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THE BLOOD IN THROMBOANGIITIS OBLITERANS

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Although thromboangiitis obliterans is considered a local vascular disease, its progressive course and the occasional general distribution of its lesions suggest a systemic origin. Increasing numbers of autopsy and clinical reports [1] indicate that almost any artery of the body may be the site of thrombosis. Bacteriologic studies [2] have not established

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1. Telford, E. D., and Stopford, J. S. B.: Thrombo-Angiitis Obliterans, Brit. M. J. **1**:863-866 (April 27) 1935. Averbuck, S. H., and Silbert, S.: Thrombo-Angiitis Obliterans: The Cause of Death, Arch. Int. Med. **54**:436-465 (Sept.) 1934. Allen, E. V., and Willius, F. A.: Disease of the Coronary Arteries Associated with Thrombo-Angiitis Obliterans of the Extremities, Ann. Int. Med. **3**:35-39 (July) 1929. Perla, D.: An Analysis of Forty-One Cases of Thrombo-Angiitis Obliterans, with a Report of a Case Involving the Coronaries and the Aorta, Surg., Gynec. & Obst. **41**:21-30 (July) 1925. Birnbaum, W.; Prinzmetal, M., and Connor, C. L.: Generalized Thrombo-Angiitis Obliterans: Report of a Case with Involvement of the Retinal Vessels and Suprarenal Infarction, Arch. Int. Med. **53**:410-422 (March) 1934. Jäger, E.: The Pathologic Anatomy of Thrombo-Angiitis Obliterans in Juvenile Gangrene of the Extremities, Virchows Arch. f. path. Anat. **284**:526-583 (May) 1932. Taube, N.: Mesenteric Involvement in Buerger's Disease, J. A. M. A. **96**:1469-1472 (May 2) 1931. Barron, M. E., and Lilienthal, H.: Thrombo-Angiitis Obliterans: General Distribution of the Disease, Arch. Surg. **19**:735-751 (Oct.) 1929. Brown, G. E.: Thrombo-Angiitis Obliterans, Surg., Gynec. & Obst. **58**:297-309 (Feb. 15) 1934. Buerger, L.: Vasomotor and Trophic Disturbances of the Upper Extremities, Am. J. M. Sc. **149**:210-229, 1915.

2. Buerger, L.: Thrombo-Angiitis Obliterans: Experimental Reproduction of the Lesions, Arch. Path. **7**:381-390 (March) 1929. Horton, B. T., and Dorsey, A. H. E.: Experimental Thrombo-Angiitis Obliterans: Bacteriologic and Pathologic Studies, ibid. **13**:910-925 (June) 1932. Rabinowitz, H. M.: Experiments on the Infectious Origin of Thrombo-Angiitis Obliterans and the Isolation of a Specific Organism from the Blood Stream, Surg., Gynec. & Obst. **37**:353-360 (Sept.) 1923.

infection as the cause of thrombosis, and neither infection nor thrombosis adequately explains the clinical and pathologic peculiarities of the disease. Homans [3] expressed the belief that the inflammatory characteristics [4] of the peripheral lesions are secondary changes due to thrombosis and to complicating infection. The lack of knowledge concerning thromboangiitis obliterans has made early diagnosis difficult and evaluation of therapeutic measures uncertain.

Changes in the circulating blood in thromboangiitis obliterans, as reported by Koga [5] in 1913, led him to believe that the vascular disease is secondary to increased viscosity of the blood. Accordingly, the treatment he recommended was directed to diluting the blood. Since then, many modifications [6] of his treatment seem to demonstrate the beneficial clinical effect accompanying a reduction in viscosity. More recent investigators [7] report various changes of the blood in thromboangiitis obliterans, either as a cause or as an effect of the disease.

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3. Homans, J.: Thrombo-Angiitis Obliterans, in A Textbook of Surgery, Springfield, Ill., Charles C. Thomas, Publisher, 1931.

4. Buerger, L.: Circulatory Disturbances of the Extremities, Philadelphia, W. B. Saunders Company, 1924; Pathology of Thrombo-Angiitis Obliterans, M. Rec. **97**:431-437 (March 13) 1920; Thrombo-Angiitis Obliterans, in Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1929, vol. 3, p. 755.

5. Koga, G.: Treatment of Spontaneous Gangrene of the Extremities, Deutsche Ztschr. f. Chir. **121**:371-382 (Feb.) 1913.

6. (*a*) McArthur, L. L.: Thrombo-Angiitis Obliterans of Buerger: Modified Koga Treatment, S. Clin., Chicago **1**:499-503 (June) 1917. (*b*) Meyer, W.: Conservative Treatment of Gangrene of the Extremities Due to Thrombo-Angiitis Obliterans, Ann. Surg. **63**:280-296 (March) 1916. (*c*) Steele, W. A.: Sodium Citrate Treatment in Thrombo-Angiitis Obliterans, J. A. M. A. **76**:429-431 (Feb. 12) 1921. (*d*) Ravinia, A., and Trosier, J.: Obliterative Endarteritis Gangrene Treated by Intravenous Injection of Sodium Citrate, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:670-682, 1924. (*e*) Silbert, S.: Treatment of Thrombo-Angiitis Obliterans, J. A. M. A. **86**:1759-1761 (June 5) 1926; Thrombo-Angiitis Obliterans: Results of Treatment with Hypertonic Salt Solution, ibid. **94**:1730-1733 (May 31) 1930; Thrombo-Angiitis Obliterans, Surg., Gynec. & Obst. **61**:214-222 (Aug.) 1935. (*f*) Rabinowitz, H. M.: The Use of Sodium Iodide Thiosulphate in the Treatment of Thrombo-Angiitis Obliterans, J. Chem. **13**:1-4 (April) 1936.

7. (*a*) Rabinowitz, H. M.: Thrombo-Angiitis Obliterans: Newer Concepts on the Physiopathology and Treatment, Am. J. Surg. **21**:260-271 (Aug.) 1933. (*b*) Rabinowitz, H. M., and Kahn, J.: Relationship of Phospholipin Metabolism to Thrombo-Angiitis Obliterans and Its Treatment, ibid. **31**:329-339 (Feb.) 1936. (*c*) Friedlander, M., and Silbert, S.: Thrombo-Angiitis Obliterans: VI. Chemistry of the Blood, Arch. Int. Med. **48**:500-506 (Sept.) 1931. (*d*) Silbert, S.; Kornzweig, A. L., and Friedlander, M.: Studies in Thrombo-Angiitis Obliterans: Reduction in Blood Volume, ibid. **45**:948-957 (June) 1930. (*e*) Bernhard, A.: Summary of the Chemical Blood Findings in Thrombo-Angiitis Obliterans, M. Rec. **97**:430-431 (March 31) 1920.

In a previous study [8] of the blood in peripheral circulatory diseases we observed an increased viscosity, a rapid coagulation and a dark, almost black color of the blood in cases of active thromboangiitis obliterans. Still more striking was the fact that the dark, venous blood from the diseased extremities was almost completely oxygenated and the carbon dioxide content in some cases was particularly low. With clinical improvement,[8a] there was a return to normal oxygen and carbon dioxide contents. It seemed to us that there existed a local or general disturbance in the dissociation of oxyhemoglobin or that the tissues were not using the oxygen supplied by the arterial blood. These observations sug-

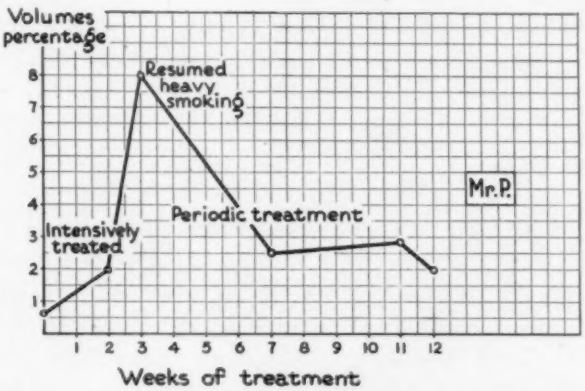

Chart 1.—Chart showing the oxygen unsaturation of the venous blood of the involved extremity of a patient with thromboangiitis obliterans. Oxygen unsaturation represents the difference between the actual oxygen content and the oxygen capacity of the blood. Normal arterial oxygen unsaturation is approximately 1 volume per cent and the average venous unsaturation 4.7 volumes per cent when the blood is withdrawn under conditions of rest. Mr. P., under stabilized conditions of rest had less than 1 volume of oxygen unsaturation of the superficial venous blood from the involved extremity as the initial determination, with an acute recurrence of the disease in the left leg. Under the same conditions, after intensive treatment the unsaturation increased to 8 volumes per cent. Subsequently, it decreased to 2 volumes per cent, and the patient admitted that he had resumed heavy smoking. Clinical improvement accompanied the evidence of increased utilization of oxygen in the superficial circulation. The right leg had been previously amputated for thromboangiitis obliterans.

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8. Theis, F. V., and Freeland, M. R.: Peripheral Circulatory Disease: Effect of Alternating Positive and Negative Pressure Treatments on Venous Blood and the Skin Temperatures, J. A. M. A. **107**:1097-1104 (Oct. 3) 1936.

8a. The patients included in this report were treated with intravenous injections of sodium thiosulfate or of sodium tetrathionate. Since February 1937 we have used almost exclusively sodium tetrathionate prepared for us experimentally and supplied by G. D. Searle & Co., of Chicago.

gested the present study to determine more fully some of the physical and chemical properties of the blood which might help in the diagnosis and the treatment of the disease.

VISCOSITY

The appearance of the blood of patients with thromboangiitis obliterans, as well as the difficulty in withdrawing it, seems to demonstrate that its viscosity is increased. The comparative values of the viscosity of the blood of patients with thromboangiitis obliterans and of normal controls reported by Koga [5] are inaccurate because of the many variable factors in the blood.[9] An increased rate of sedimentation during the active stage of the disease interfered with the accepted Hess method [10] for determinations of viscosity. It was apparent that the passage of whole blood through the Hess tube was delayed by the rapid settling of the cellular constituents. Consequently, comparative values of the viscosity of the blood could not be established by capillary tube methods.

SEDIMENTATION TESTS

In attempting these tests for viscosity, we felt that some data on the sedimentation rate of patients with thromboangiitis obliterans should be available. The Linzenmeier method [11] was used, and from two to four hours or more was accepted as the time for 18 mm. of cells to settle in normal blood. Seven persons with active thromboangiitis obliterans had rates of from fifteen to forty-five minutes (table 1). No evidence of infection was present to account for the rapid sedimentation. In contrast, ten tests on clinically recovered or improved patients with thromboangiitis obliterans showed sedimentation rates as high as nine hours. Ten patients with other peripheral circulatory diseases had sedimentation rates varying from an hour and two minutes to more than five hours. The difference between the sedimentation rates of persons with acute or active thromboangiitis obliterans and those of improved or recovered patients seems to be of diagnostic and prognostic significance.

HEMATOCRIT TESTS

Increased cell volume due to anhydremia or to polycythemia was considered a possible factor in the increased viscosity and increased sedi-

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9. Burton-Opitz, R.: The Viscosity of the Blood, J. A. M. A. **57**:353-358 (July 29) 1911. Samuels, S. S.: Diagnosis and Treatment of Diseases of the Peripheral Arteries, New York, Oxford University Press, 1931, p. 60.

10. Hess, W. R.: A New Apparatus for Determining Blood Viscosity, München. med. Wchnschr. **54**:1590-1591 (Aug. 6) 1907. Bircher, M. E.: Clinical Diagnosis by the Aid of Viscosity of the Blood and Serum, J. Lab. & Clin. Med. **7**:134-147 (Dec.) 1921.

11. Bray, W. E.: Synopsis of Chemical Laboratory Methods, St. Louis, C. V. Mosby Company, 1936.

mentation time. Accordingly, hematocrit tests were made to determine the actual percentage volume of cells and of serum. With a graduated tube, the blood was centrifuged for forty-five minutes at a predetermined rate to produce maximum packing of the cells. Observations (table 2) on patients with various types of peripheral circulatory diseases and on normal controls did not show a significant increase in cell volume for those with thromboangiitis obliterans. In general, a direct relation between the cell volume and the red cell count is to be expected if the

TABLE 1.—*Sedimentation Time of the Blood of Patients with Thromboangiitis Obliterans and with Other Peripheral Circulatory Diseases (Linzenmeier Method)*

	No. of Patients	Time: Maximum Hr.	Maximum Min.	Minimum Hr.	Minimum Min.	Average Hr.	Average Min.
Thromboangiitis obliterans							
Acute or active stage	7	0	45	0	15	0	30
Improved or clinically recovered	10	9	30	1	5	3	54
Other peripheral circulatory diseases	10	5	45	1	2	3	0

TABLE 2.—*Hematocrit or Packed Cell Volume Percentage of Patients with Peripheral Circulatory Diseases*

	No. of Patients	Maximum Cell Vol. %	Minimum Cell Vol. %	Average Cell Vol. %
Controls—normals and others	40	54.00*	32.52	39.58
Thromboangiitis obliterans	40	50.53	33.33	43.28
With anemia	..	39.60	33.33	35.37
With polycythemia	..	50.53	40.49	46.06
Polycythaemia vera—no thrombosis	2	62.63	56.66	59.64
Thrombophlebitis				
Migrating	1	44.75	43.21	43.73
Spontaneous	6	45.76*	37.10	42.33
Arteriosclerosis				
Senile	9	40.00	34.07	36.45
Diabetic	1	.....	.....	39.60
Raynaud's disease and neurocirculatory diseases	10	44.26	33.19	38.06
Frostbite	4	41.33	38.20	39.86

* Heavy smokers.

size of the cells remains constant. This was usually found to be true except in the cases of thromboangiitis obliterans, in which high cell counts were frequently present with low cell volumes. One patient with repeated red cell counts over 5,500,000 had volume percentages under 35. Subsequently, with a normal cell count of 4,600,000, he had a normal cell volume of 40 per cent. The reverse of these conditions was also noted in that low cell counts occurred with a higher than normal cell volume. These observations in cases of thromboangiitis obliterans indicate that the size of the erythrocytes fluctuates during the course of the disease and that the increased viscosity of the blood is not due to high cell volume as a result of anhydremia or of polycythemia.

HEMOGLOBIN AND CELL COUNTS

The frequency of high red cell counts in the cases of thromboangiitis obliterans at some time during the period of observation suggested polycythemia as a stage of the disease (table 3). In the acute stage, the cell counts were usually around 4,000,000, while during the period of

TABLE 3.—*Hemoglobin Content and Blood Counts in Patients with Peripheral Circulatory Diseases*

Erythrocyte Counts of Patients with Thromboangiitis Obliterans

Patients	No. of Counts	Period of Observation, Months	In Millions: Maximum	In Millions: Minimum	In Millions: Average
Mr. Pl.	6	2	6.35	5.30	5.90
Mr. V.	4	5	5.15	4.12	4.49
Mr. P.	2	12	4.85	4.67	4.76
Mr. A.	8	13	6.04	4.80	5.40
Mr. Bo.	9	39	5.62	4.36	5.01
Mr. S.	2	1½	3.96	3.61	3.79
Mr. B.	5	22	5.60	4.14	4.89
Mr. El.	5	25	4.75	4.15	4.50
Mr. K.	5	90	5.67	3.92	4.63
Mr. J.	7	12	5.66	4.19	4.68
Mr. R.	4	7	5.85	4.84	5.18
Mr. O.	9	11	4.80	3.68	4.03
Mr. M.	9	38	5.27	3.96	4.36
Mr. C.	8	27	5.75	4.41	5.21
Mr. N.	13	39	7.58	3.91	5.17
Mr. N.	4	8	6.00	4.19	4.97
Mr. L.	7	12	5.23	4.23	4.85
Mr. Sm.	4	7	5.85	4.56	5.11
Mr. E.	1	2	5.34	....	....
Mr. Ch.	3	34	5.90	5.20	5.66
Mr. Al.	2	1	5.41	5.11	5.26

	No. of Patients	No. of Patients with Maximum Counts (In Millions) Over: 4.0	5.0	5.5	6.0	7.0
Thromboangiitis obliterans	21	4	4	9	3	1
Other peripheral circulatory diseases	65	46	10	0	0	0
Polycythaemia vera	2	0	0	0	1	1

Leukocyte Counts

	No. of Patients	No. of Patients with Maximum Counts Over: 6,000	12,000	15,000
Thromboangiitis obliterans	20	3	15	2
Other peripheral circulatory diseases	49	41	7	1
Polycythaemia vera	2	2	0	0

Hemoglobin Determinations

	No. of Patients	No. of Patients with Percentage Over: 80	90	100	105	110
Thromboangiitis obliterans	20	4	4	9	1	2
Other peripheral circulatory diseases	49	36	10	2	0	0
Polycythaemia vera	2	0	1	1	0	0

clinical improvement, normal counts or counts showing polycythemia were noted. Of 21 patients, 17, or 81 per cent, had one or more counts over 5,000,000; of these, 13, or 62 per cent, had counts over 5,500,000. One patient had two low red cell counts, but he was observed for less than two months. Of 65 persons with other circulatory diseases, only 10, or 15 per cent, had counts slightly over 5,000,000, and the counts of 9 persisted under 4,000,000. The condition of 2 patients was diagnosed

as polycythaemia vera with circulatory symptoms, but these patients were not included in the group of those with thromboangiitis obliterans because of the absence of thrombosis. The fact that the red cell counts of patients with thromboangiitis obliterans change during the course of the disease indicates a stage of anemia and a stage of polycythemia.

In the absence of infection, increased white cell counts usually accompany the higher red cell counts. Increase in both the red and the white cells would seem to be evidence of increased concentration of the blood in the stage of polycythemia but would not account for the greater viscosity of the blood or for the more rapid sedimentation during the acute stage of the disease when counts are normal or low.

Determinations of hemoglobin were made by the Newcomer method. Variations in the content of hemoglobin were found in the same patient with thromboangiitis obliterans without changes in red cell counts. High percentages were more frequent in patients with thromboangiitis obliterans than in normal controls or in patients with other circulatory diseases and usually accompanied normal cell counts and clinical improvement.

COAGULATION OF THE BLOOD

The rapid and firm coagulation of the blood of patients with acute thromboangiitis obliterans is particularly striking as the blood is emptied from a syringe. In a number of instances, the clotting occurred so quickly and so solidly that all efforts to remove the plunger from the syringe failed. With the use of fine capillary tubes, the coagulation time of patients with acute thromboangiitis obliterans was frequently found to be less than one minute, increasing to two or more minutes as the patient improved. The rapid clotting is not due to an increase of calcium in the serum, for the calcium and phosphorus in the serum were always within normal limits. Furthermore, in one determination of fibrinogen the content was below normal.

REACTION OF THE BLOOD

Changes in the reaction of the blood affect the size of the red corpuscles.[12] As previously described, changes in the size of the erythrocytes occur in thromboangiitis obliterans. Accordingly, a shift in the acid-base balance could produce such changes. Theoretic p_H's from Bock's monograms [13] were obtained by using the oxygen content and

12. Price-Jones, C.: The Diurnal Variations in the Sizes of Red Blood Cells, J. Path. & Bact. **23**:371-383 (Dec.) 1920.

13. (*a*) Bock, A. V.; Dill, D. B.; Hurxthal, L. M.; Lawrence, J. S.; Coolidge, T. C.; Dailey, M. E., and Henderson, L. J.: Blood as a Physicochemical System: V. The Composition and Respiratory Exchanges of Normal Blood During Work, J. Biol. Chem. **73**:749-766 (June) 1927. (*b*) Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry: Interpretations, Baltimore, Williams & Wilkins Company, 1932, vol. 1.

the carbon dioxide content of the blood. In 5 cases of acute thromboangiitis obliterans, the initial p_H thus obtained was 7.60 or higher. However, these values are greater than any that actually occur, because of buffer substances compensating for abnormal oxygen content and for abnormal carbon dioxide content. We are now able to get actual potentiometric p_H's, both with glass and with quinhydrone electrodes, which compare fairly accurately with the nomogram values. As a rule, the actual p_H is about 0.06 less than the aforementioned theoretic values. Our most recent determinations showed actual p_H's of 7.60, 7.62 and 7.64, with theoretic values beyond the range of the nomograms. A p_H of from 7.38 to 7.50 was uniformly obtained for normal controls, for clinically recovered or improved patients with thromboangiitis obliterans and for patients with other peripheral circulatory diseases. For patients with acute thromboangiitis obliterans, the p_H was consistently higher and above 7.55. Such changes in the reaction of the blood in long-standing conditions such as thromboangiitis obliterans, whether a cause or an effect of the disease, reflect a general shift of the buffer substances as well as changes in the metabolic processes of the body.

OXYGEN AND CARBON DIOXIDE CONTENTS OF THE BLOOD

Determinations of the oxygen and the carbon dioxide content of the blood were made by the Van Slyke technic [14] with and without reagents. Patients were stabilized at rest in bed for one hour or more, and, without the use of a tourniquet, the blood was withdrawn under oil from the antecubital vein at the elbow or from a branch of the internal saphenous vein at the knee. The specimens were immediately transferred to mercury tonometers, placed in a refrigerator and analyzed as soon as possible. All determinations were made in duplicate, and careful checks established the accuracy of the procedures. Difficulty in finding superficial veins in many patients with thromboangiitis obliterans made it impossible to obtain blood from both the arm and the leg in every case. The data included in the tabulations in table 4 pertain to patients from whom blood could be withdrawn from the involved extremity.

Gasometric Method with Reagents.—In a series of 7 patients with acute or recurrent thromboangiitis obliterans, determination of the oxygen and the carbon dioxide content of the venous blood from the involved extremity showed arterial oxygenation (table 4). Patients with other circulatory diseases and clinically recovered or improved patients with thromboangiitis obliterans had normal values with from 15 to 40 per cent oxygen unsaturation.[15] Usually, the uninvolved extremi-

14. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry: Methods, Baltimore, Williams & Wilkins Company, 1932, vol. 2.

15. Lundsgaard, C.: Studies of Oxygen in the Venous Blood: I. Technique and Results in Normal Individuals, J. Biol. Chem. **33**:133-144 (Jan.) 1918.

ties had values which were either normal or lower than normal. The blood from the involved extremity should be studied because the oxygen and carbon dioxide contents in the arm usually differ from those in the leg of the same patient (table 5). In the presence of poor circulation, these conditions indicate a local disturbance in the utilization of oxygen in the involved extremity. In some instances, however, almost complete oxygen saturation of the venous blood from apparently unaffected extremities was also present, which indicated that high oxygen saturation of the venous blood may be either a local or a general condition.

Arterial oxygen content of the venous blood occurs either with a rapid flow of blood or with nonutilization of the oxygen supplied by the arterial blood. Meakins and Davies[16] demonstrated that submerging a normal extremity in water at 45 C. will increase the rate of blood flow so that the oxygen content of the venous blood is the same as

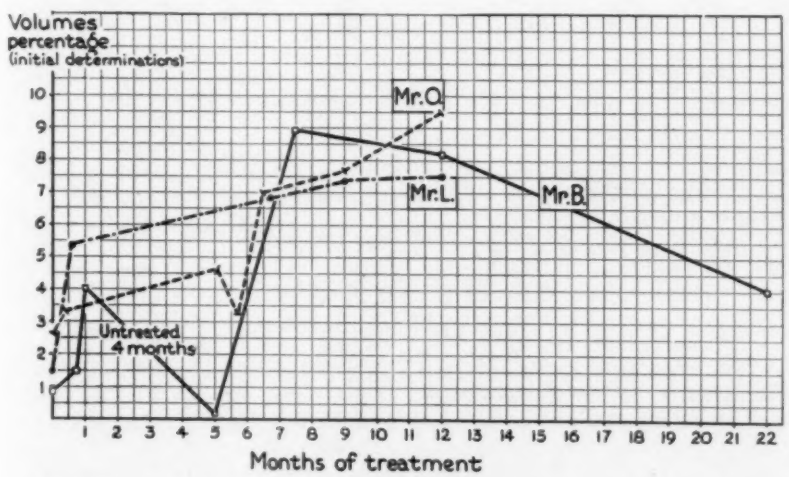

Chart 2.—Chart showing the oxygen unsaturation of the venous blood of the involved extremity of 3 patients with thromboangiitis obliterans. The curves represent the utilization of oxygen in the superficial circulation in the involved extremity under the same conditions as those described in chart 1. The 3 patients were observed for from twelve to twenty-two months, and the initial determinations on the venous blood were the same as those usually found in the arterial blood (table 4). With clinical improvement, normal or higher than normal oxygen unsaturation continued, except in the case of Mr. B. After four months without treatment, he had a painful recurrent ulcer on the first toe, and there was a return of the high oxygen saturation of the venous blood. Relief from pain and rapid healing of the ulcer accompanied greatly increased unsaturation of the venous blood. The almost complete oxygen saturation of the venous blood in the presence of poor circulation indicates nonutilization of oxygen by the tissues.

16. Meakins, J. C., and Davies, H. W.: Observations on the Gases in Human Arterial and Venous Blood, J. Path. & Bact. **23**:451-461 (Dec.) 1920.

that of the arterial blood. This condition of rapid blood flow was certainly not present in the cases of thromboangiitis obliterans. As shown in table 4, the subnormal stabilized skin temperatures taken by means of a

TABLE 4.—*Initial Determinations of Oxygen and Carbon Dioxide Contents of Venous Blood and Peripheral Skin Temperature of Involved Extremity of Patients with Thromboangiitis Obliterans and Other Peripheral Circulatory Diseases*

Initial Determinations for Patients with Acute Thromboangiitis Obliterans

	Involved Extremity	O_2 Capacity, Vol. %	O_2 Saturation, %	CO_2 Content, Vol. %	Average Temperature of Toes or Fingers
Mr. P.	L. leg	21.65	96.6	22.50	28.6 C.
Mr. R.	R. leg	20.38	95.8	37.74	25.2 C.
Mr. B.	R. leg	23.90	96.5	39.77	27.1 C.
Mr. C.	L. leg	21.10	98.0	46.66	30.0 C.
Mr. K.	R. leg	18.85	94.7	49.91	27.8 C.
Mr. M.	R. arm	19.00	92.7	42.30	26.7 C.
Mr. L.	L. leg	18.50	91.9	44.56	30.0 C.

Average Initial Determinations for All Subjects

	No. of Patients	O_2 Capacity, Vol. %	O_2 Saturation, %	CO_2 Content, Vol. %
Controls				
Normal	9	19.38	72.15	49.79
Others	7	19.30	69.28	49.89
Thromboangiitis obliterans				
Initial—untreated	7	19.97	95.32	40.53
Clinically recovered	11	18.13	62.53	49.83
Other peripheral circulatory diseases	19	18.17	68.05	48.56
Polycythemia—with peripheral circulatory symptoms but no thrombosis	2	22.48	73.95	46.71

TABLE 5.—*Difference in Oxygen and Carbon Dioxide Contents of the Venous Blood of the Leg and Arm of One Patient*

	Leg, Contents, Vol. %		Arm, Contents, Vol. %	
Date	O_2	CO_2	O_2	CO_2
3/23/36	11.61	45.75	8.68	48.77
4/ 6/36	14.81	39.95	9.34	43.40
4/ 7/36	13.79	41.39	8.68	41.68
4/ 8/36	9.07	45.84	5.13	48.40
4/13/36	18.00	37.10	8.54	44.47
Average	13.46	42.00	8.07	45.34

Tycos dermatherm [17] indicate a diminished flow of blood. With a diminished or sluggish flow, there should be more oxygen withdrawn from the blood and more carbon dioxide absorbed by the blood.[15] Accordingly, the reverse of what was actually found is expected in a sluggish circulation. Nonutilization of oxygen by the tissues would account for the arterial oxygen content of the venous blood in the pres-

17. Scott, W. J. M.: An Improved Electrothermal Instrument for Measuring Surface Temperature, J. A. M. A. **94**:1987-1988 (June 21) 1930.

ence of a low skin temperature. This agrees with Popoff's histologic study [18] that in thromboangiitis obliterans abnormal communications or anastomoses shunt the arterial blood directly into the veins without irrigating the capillaries of the tissues. However, our findings of the normal utilization of oxygen with clinical improvement do not support Popoff's irreversible process.

Vacuum Method.—In order to determine the stability of the oxygen and the hemoglobin in the blood, we studied the dissocation of the two by means of vacuum only. No reagents were used in the Van Slyke reaction chamber. For 15 controls, an average of 66.91 per cent of the oxygen was liberated; for 5 patients with thromboangiitis obliterans 68.70 per cent, and for 3 with arteriosclerosis, 58.04 per cent. These results showed that in the cases of thromboangiitis obliterans the oxyhemoglobin in the blood released a normal amount of oxygen when subjected to vacuum only.

METHEMOGLOBIN

The initial high oxygen saturation and the dark color of the venous blood in the involved extremity of the patients with thromboangiitis obliterans suggested the possibility of some inactive form of oxygen and hemoglobin. One form, methemoglobin, is dark colored and liberates its oxygen much less readily than does oxyhemoglobin.[19] Results of spectroscopic examinations were repeatedly negative for methemoglobin, but less than 25 per cent methemoglobin has been reported as insufficient concentration [20] to be discernible spectroscopically. Therefore, ten quantitative determinations were made by the Stadie method.[21] The occasional presence of small amounts of methemoglobin was too insignificant for it to be a factor in the abnormal condition of the blood in thromboangiitis obliterans.

METABOLISM TESTS

It seemed questionable whether these observations of disturbed utilization of oxygen would materially affect the total oxygen consumption of the body and, consequently, the basal metabolic rate. However,

18. Popoff, N. W.: The Digital Vascular System, with Reference to the State of the Glomus in Inflammation, Arteriosclerotic Gangrene, Diabetic Gangrene, Thrombo-Angiitis Obliterans and Supernumerary Digits, Arch. Path. **18**:295-330 (Sept.) 1934.

19. Conant, J. B., and Fieser, L. F.: Methemoglobin, J. Biol. Chem. **62**:595-622 (Jan.) 1924. Conant, J. B., and Scott, M. D.: The So-Called Oxygen Content of Methemoglobin, ibid. **69**:575-587 (Aug.) 1926. Anson, M. L., and Mirsky, A. E.: On Hemochromogen and the Relation of Protein to the Properties of Hemoglobin, J. Physiol. **60**:50-67 (May 21) 1925.

20. Kobert, R.: Lehrbuch der Intoxikationen, ed. 2, Stuttgart, Ferdinand Enke, 1902, vol. 1, p. 97; cited by Peters and Van Slyke,[13b] p. 635.

21. Stadie, W. C.: Method for Determination of Methemoglobin in Blood, J. Biol. Chem. **41**:237-241 (Feb.) 1920.

Silbert and Friedlander [22] reported low metabolic rates for 50 unselected patients with thromboangiitis obliterans, and for none was the rate above zero; the average for smokers and nonsmokers was — 16 per cent. In the absence of infection or of severe pain, the rates for our patients were as low as — 27 per cent, and all were persistently below zero. Coller and Maddock [23] studied the relation of metabolic rates to peripheral temperatures and stated that low body metabolism probably accounts for low peripheral skin temperatures. Our results confirm the presence of low basal metabolic rates in cases of uncomplicated thromboangiitis obliterans.

COMMENT

The increased viscosity and the rapid clotting of the blood in acute thromboangiitis obliterans may be the important factors in the complex physiology of the blood which leads to thrombosis. Meyer [6b] advised treatment with a solution of sodium citrate to overcome the rapid clotting; whether the various salt solutions act as anticoagulants, as diluents or by shifting the acid-base balance in the blood and tissues has not been determined. The adequacy or availability of oxygen in the internal organs of the body influences the rapidity of coagulation. Rapid clotting during asphyxia, according to Cannon and Mendenhall,[24] is the result of deficient oxygen supply; and Gray and Lunt [25] attributed the rapid coagulation which follows moderate hemorrhage as due to the same deficiency. Accordingly, the evidence of anoxia or disturbed utilization of oxygen here presented should affect the coagulation of the blood and contribute to thrombus formation.

Anoxia, or lack of oxygen, in the tissues of the involved extremity of patients with acute thromboangiitis obliterans is not due entirely to arterial occlusion. The almost complete oxygen saturation of the superficial venous blood indicates either a failure of the arterial blood to irrigate the tissues or an inability of the tissue cells to utilize the oxygen supply. The normal utilization of oxygen by improved or recovered patients does not support Popoff's [18] irreversible process of direct arterial-venous shunting of the blood in this disease. Rest pains and intermittent claudication are clinical evidence of the oxygen want; the severity of the symptoms is frequently out of all proportion to the

22. Silbert, S., and Friedlander, M.: Studies in Thrombo-Angiitis Obliterans: The Basal Metabolism, J. A. M. A. **96**:1857-1858 (May 30) 1931.

23. Coller, F. A., and Maddock, W. G.: Function of Peripheral Vasoconstriction, Ann. Surg. **100**:983-992 (Nov.) 1934.

24. Cannon, W. B., and Mendenhall, W. L.: Factors Affecting the Coagulation Time of Blood, Am. J. Physiol. **34**:243-250 and 251-261 (March) 1914. Cannon, W. B., and Gray, H.: Factors Affecting the Coagulation Time of Blood, ibid. **34**:232-242 (March) 1914.

25. Gray, H., and Lunt, L. K.: Factors Affecting the Coagulation Time of Blood, Am. J. Physiol. **34**:332-351 (June) 1914.

oxygen want of the tissues, due to arterial occlusion [26] or to the degree of circulatory deficiency.

The normal or anemic blood cell counts during the painful stage of the disease are replaced by higher red cell counts during the stage of recovery. This important compensatory reaction of the hemopoietic system to oxygen want in other diseases has been thoroughly studied by Barcroft.[27] Eighty-one per cent of our patients had erythrocyte counts of from 5,000,000 to 7,500,000. In other types of peripheral circulatory diseases, irrespective of the degree of oxygen deficiency or of gangrene due to arterial occlusion, red cell counts were rarely above normal and usually continued below normal. In thromboangiitis obliterans these apparently compensatory changes in red cell counts have not been considered in relation to the stages of the disease. According to Piney,[28] low red cell counts may occur in polycythaemia vera, and Lamson [29] described red cell counts over 5,000,000 as indicative of polycythemia, oxygen want being the fundamental cause [30] of the increased cell counts. The similiarity of polycythaemia vera and thromboangiitis obliterans as observed in the hematologic clinic of the New York Hospital has been reported recently.[31] Pernokis [32] found that peripheral circulatory symptoms were present in 75 per cent of his cases of polycythaemia vera. The frequency of arterial thrombosis in polycythaemia vera is more generally known than is the occurrence of secondary polycythemia in thromboangiitis obliterans.

Fluctuation in the size of the erythrocytes occurs in thromboangiitis obliterans, which is probably due to changes in the reaction of the blood. In the acute stage, the blood is more alkaline than in any other stage, but the carbon dioxide–combining power of the blood as an index of acid-base balance is not above normal limits. Normally, the cell volume

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26. Theis, F. V.: Artery and Concomitant Vein Ligation in Surgery of the Large Blood Vessels, Arch. Surg. **17**:244-258 (Aug.) 1928. Horton, B. T.: A Study of the Vessels of the Extremities by the Injection of Mercury, S. Clin. North America **10**:159-170 (Feb.) 1930. Brown, G. E.: Thrombo-Angiitis Obliterans, Surg., Gynec. & Obst. **58**:297-309 (Feb. 15) 1934.

27. Barcroft, J.: The Respiratory Function of the Blood, London, Cambridge University Press, 1925, vol. 1; 1928, vol. 2.

28. Piney, A.: Diseases of the Blood, Philadelphia, P. Blakiston's Son & Co., 1932, p. 160.

29. Lamson, P. D.: Polycythemia, in Nelson Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1920, vol. 4; Role of the Liver in Acute Polycythemia, J. Pharmacol. & Exper. Therap. **7**:169-224 (July) 1915.

30. Fitz, R.: Polycythemia, in Christian, H. A., and Mackenzie, J.: Oxford Medicine, New York, Oxford University Press, 1924, vol. 2.

31. Reznikoff, P.; Foot, N. C., and Bethea, J. M.: Etiologic and Pathologic Factors in Polycythemia Vera, Am. J. M. Sc. **189**:753-759 (June) 1935.

32. Pernokis, E. W.: Blood Studies, J. A. M. A. **108**:1686-1690 (May 15) 1937.

percentage is related to changes in the cell counts. However, in thromboangiitis obliterans the high, or polycythemic counts with lower than normal cell volume do not support the opinion [7d] that the increased viscosity of the blood is due to anhydremia, unless the size of the red cells is reduced to a greater extent than the reduction in serum volume.

Other blood changes [7] have been reported. We have been able to confirm the observations of Rabinowitz and Kahn on disturbed phospholipin metabolism, of Silbert and Friedlander on cholesterol and of Bernhard on disturbances in sugar metabolism. Four of our patients had transient glycosuria with normal blood sugar. These observations, as well as the success of treatment with intravenous solutions, are predominantly in favor of naming disturbed physiology of the blood, leading to increased coagulation and formation of thrombi, as the important underlying condition in thromboangiitis obliterans.

The diagnosis of thromboangiitis obliterans, either clinical or pathologic, is based primarily on the presence of peripheral arterial occlusion. Autopsy [33] has demonstrated the distribution, the extent and the characteristics of the vascular lesions, but the cause of the thromboses is not explained by the pathologic changes. The majority of patients have the recurrnet progressive disease described by Buerger; [4] the condition in many cases remains permanently arrested or cured. We have no reason to assume that the disease is due to the same cause in all instances. Goodman's [34] contention that thromboangiitis obliterans is caused by the Rickettsia of typhus fever is untenable. In 6 cases included in this investigation, cutaneous tests with antigen supplied by Goodman were all negative.

Our purpose in this investigation was to find some means of making an early diagnosis, to evaluate the effectiveness of treatment and to determine when the disease has been arrested. Those factors in the complex physiology of the blood which seemed most pertinent to the clinical and pathologic pictures of the disease were included in this investigation. We believe that the definitely pathologic condition of the blood during the acute or painful stage of the disease, which for the most part returns to normal with clinical recovery, offers a sound basis for future study. Further studies we are now making should disclose other changes in the blood and some of the factors controlling local oxidation of tissue.

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33. Morgan, J. R. E.: Thrombo-Angiitis Obliterans: Distribution of the Lesions in the Vessels of the Leg, Arch. Path. **18**:216-224 (Oct.) 1934. Telford, E. D., and Stopford, J. S. B.: Thrombo-Angiitis Obliterans, Brit. M. J. **2**:1035-1037 (Dec. 6) 1924. Buerger.[4]

34. Goodman, C.: Thrombo-Angiitis Obliterans and Typhus: Evidence of Etiologic Relationship, Arch. Surg. **35**:1126-1144 (Dec.) 1937.

SUMMARY AND CONCLUSIONS

In a series of 7 cases of acute thromboangiitis obliterans in which the superficial venous blood from the involved extremity could be studied, we found increased viscosity of the blood, rapid sedimentation of the cells, rapid coagulation, greatly increased alkalinity, low or normal cell counts and arterial oxygen saturation and a low carbon dioxide content of the blood.

In 21 clinically improved or recovered patients with thromboangiitis obliterans, in normal controls, and in patients with other peripheral circulatory diseases, these conditions were not present.

Clinical improvement with relief from rest pains in cases of thromboangiitis obliterans is accompanied by normal oxygen saturation of the venous blood and usually by a normal or polycythemic blood count.

With recurrence of the disease, we found a return to the high oxygen saturation of the venous blood.

These results suggest that a disturbance in the utilization of oxygen is one of the conditions in the complex physiology of the blood and tissue metabolism which are responsible for the acute symptoms of thromboangiitis obliterans.

At present, a thorough study of the chemical and physical properties of the blood is necessary (1) to make an early diagnosis of thromboangiitis obliterans, (2) to evaluate the effectiveness of treatment and the harmful effect of contributing factors such as smoking, (3) to detect recurrences, and (4) to determine when the disease has been arrested.

Miss Bernice Rhodes, of the Department of Bacteriology, and Miss Helen Higgins and Mr. Arthur Nielsen, of the Department of Peripheral Circulatory Diseases, Presbyterian Hospital, assisted us in this study.

SERUM THERAPY FOR STREPTOCOCCIC INFECTION OF THE NOSE, THROAT AND EAR AND ITS COMPLICATIONS

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In our earlier series[1] of 26 patients treated with serum, 8 were allocated to the category of patients with diseases of the ear, nose and throat. Cultures of the blood of 6 of these yielded bacteria. Two died and 6 survived. In our present additional group of 66 patients, data on whom were tabulated in the immediately preceding paper of the present series, 30 patients were assigned to this category, including patients with pneumonia, empyema and mediastinitis. Their cases will here be designated by the serial numbers employed in the general tabulation in the preceding paper of this series.[2]

CASE 29.—R. C., a boy aged 14, contracted a head cold on Oct. 16, 1933, and later had purulent otitis media. About October 25 the temperature rose to 105 F. and remained high until the boy's admission to the hospital, on October 30. A culture of blood taken on October 28 gave a positive growth of hemolytic streptococci. A mastoidectomy on the right side had been done in 1930. A culture of blood taken October 30 again yielded bacteria, and on October 31 the concentrated streptococcus serum of the New York state department of health was given, the total amount being 18,900 units. A mastoidectomy on the left revealed a thrombus in the left lateral sinus. The left internal jugular vein was ligated, and a transfusion of 260 cc. of blood was given. Intravenous serum treatment was continued; 60,000 units was given on November 1; 20,000 units on November 2; 20,000 units on November 3; 60,000 units on November 4; 40,000 units on November 5, and 40,000 units on November 6. A culture of blood taken on this day remained sterile, and because of this fact and the distressing urticaria the serum was discontinued. However, a culture of blood taken on November 8 gave a positive growth on November 9, and the serum was again given, in divided

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1. Sheplar, A. E.; Spence, M. J., and MacNeal, W. J.: Therapeutic Use of the Concentrated Streptococcus Serum of the New York State Department of Health in Patients with Infections of the Ear, Nose and Throat, Arch. Surg. **30**:1-13 (Jan.) 1935.

2. Sheplar, A. E.; Spence, M. J., and MacNeal, W. J.: General Observations on the Serum Therapy of Infections with Streptococcus, Arch. Surg. **35**:772-789 (Nov.) 1938.

doses, to a total of 30,000 units. Severe cyanosis and dyspnea occurred in spite of care in administration. The serum was continued daily until November 16. On November 29 an abscess of the right arm was incised, and the pus contained hemolytic streptococci. A transfusion of 180 cc. was given. On December 3 a small abscess in the right groin was aspirated; it yielded pus containing staphylococci. On December 7 a thoracentesis on the left yielded 250 cc. of fluid containing hemolytic streptococci, but this empyema cleared without further drainage. A transfusion of 200 cc. was given on December 11. The patient was discharged December 24 and has remained well up to the time of writing. A total of 355,400 units of New York state concentrated serum was used.

CASE 33.—B. F., a boy aged 5 years, was admitted to the hospital Jan. 12, 1934, with otitis media on the left. Spinal tap on January 12 yielded fluid containing hemolytic streptococci. The concentrated streptococcus serum was given by intrathecal and intravenous injection from January 14 to January 21, to a total of 460,000 units. The patient died on January 23, and necropsy revealed generalized purulent meningitis and bronchopneumonia of the lower lobe of the right lung.

CASE 34.—C. F., a boy, born July 30, 1932, had a history of mastoidectomy on the right in December, at the age of 5 months. Subsequently there was slowly progressive osteomyelitis of the skull, which was found to be due to Staphylococcus aureus. The treatment of this condition is not of concern here, but on Jan. 17, 1934, complicating purulent otitis media on the left side, caused by Streptococcus haemolyticus, was recognized. The grave condition of the patient precluded operative intervention. The concentrated streptococcus serum (New York state) was given daily from January 17 to 26, to a total of 18,900 units, and the left ear healed promptly.

CASE 37.—K. B., a girl aged 7 years, was admitted to the hospital Feb. 12, 1934. The right ear drum had been incised on January 29, and since February 8 there had been several chills and a rise of temperature to 106 F. The left hip was rigid and tender. Cultures of blood taken on February 12, 13 and 14 gave positive growth of hemolytic streptococci. A mastoidectomy on the right was performed on February 13, and a transfusion of 350 cc. of blood was given. The administration of concentrated streptococcus serum (New York state) was started on February 14 and continued daily to February 22, except for one day (February 18), the total amount being 240,000 units. The general progress was favorable, and the patient was able to sit in a wheel chair on March 3. The left hip continued painful, and a roentgenogram revealed epiphysitis at the upper end of the left femur. Aspiration and drainage of the left hip joint on March 15 yielded 60 cc. of pus containing streptococci. The patient was discharged on April 9, with a plaster dressing still in place.

CASE 39.—J. M., a boy aged 10 years, was seen in consultation at a hospital in Westchester County on April 7, 1934. He had had purulent otitis media on the right on March 14, and a culture of material from this ear was reported as yielding staphylococci. Culture of material taken from the throat at the same time showed predominant streptococci. On April 1 there was double vision in the right eye. A simple mastoidectomy on the right released a considerable amount of pus. After the operation the temperature reached 105.6 F. On April 6 there were signs of meningeal irritation, and spinal puncture yielded cloudy fluid containing 1,650 leukocytes per cubic millimeter. A culture of this fluid remained sterile. When the patient was seen on April 7 his condition was considered

desperate. The spinal fluid on this day contained about 2,000 white cells per cubic millimeter, but bacteria could not be recognized in it by microscopic study and the cultures remained sterile. The mastoidectomy wound was explored, with exposure of the lateral sinus and of the dura. This wound was irrigated with staphylococcus bacteriophage. Concentrated streptococcus serum (New York state) was given, 10 cc. into the spinal canal and 10 cc. intravenously. A transfusion of 200 cc. of blood was also given. On April 8 the spinal fluid was bloody and contained 2,800 white cells per cubic millimeter. The intraspinal and intravenous doses of streptococcus serum were repeated. On April 10 an intravenous injection of 10 cc. of serum was given. On April 12 the spinal fluid contained 1,050 white cells per cubic millimeter. Another intraspinal injection of 10 cc. of serum was given. On April 14 the temperature came down to normal, and the patient made a complete recovery. All cultures of the spinal fluid remained sterile. The precise condition within the skull remains, therefore, somewhat uncertain. It would seem from the clinical evidence that the infection was probably due to Str. haemolyticus and that it was close to the establishment of a generalized infection of the meninges when the serum treatment was started.

Case 42.—L. I., a girl aged 4½ years, was admitted to the hospital on June 4, 1934, with a history of discharge from the right ear for two weeks and also of vomiting, fever and pain in both ankles, the right calf and the left knee for the last five days. On June 4 the temperature reached 105.6 F., and a culture of blood taken on this day gave an abundant growth of Str. haemolyticus. Daily cultures of the blood on June 5, 6, 7 and 8 yielded bacteria but a culture of blood taken June 9 remained sterile. On June 5 a mastoidectomy and ligation of the jugular vein were performed on the right and a transfusion of 135 cc. of blood was given. Concentrated streptococcus serum (New York state) was given intravenously, 40,000 units on June 6, 20,000 units intravenously and 20,000 units into muscle on June 7, 80,000 units intravenously on June 8 and 40,000 units on June 9. Because of the sterility of the culture the serum was now discontinued. Severe urticaria appeared on June 11 and persisted for two days. The patient appeared improved. After a transfusion of 200 cc. of blood on June 16 the temperature rose to 102.2 F., and a culture of blood taken on June 18 again revealed streptococci in the blood stream. Another culture, made on June 20, likewise yielded bacteria. A transfusion of 200 cc. of blood was given on June 21. Arthritis of the left hip and left knee was treated by traction and immobilization in a plaster dressing. The patient was discharged on July 26, without any disability. The total amount of serum used was 200,000 units.

Case 48.—E. C., a man aged 30, was admitted to the hospital on Sept. 29, 1934, at which time an abscess of the thyroid gland was incised and drained. At this time roentgenographic examination indicated a tumor in the superior mediastinum. The patient was again admitted on October 14, at which time a tracheal intubation was done and a second abscess, between the trachea and the manubrium sterni, was incised and drained. He was discharged on October 20 and returned on November 18, at which time the wound was reopened and drained. Discharged on November 23, he returned again on November 26. More pus was evacuated through the wound above the manubrium sterni. Culture of the pus showed predominating hemolytic streptococci, smaller numbers of staphylococci and diphtheroids. A roentgenogram taken on November 27 revealed a mediastinal mass with a large cavity in it. On November 28 the patient was dyspneic and uncomfortable. His temperature reached 104 F. A culture of blood taken at this time remained sterile. On November 29 concentrated streptococcus serum (New York state) was given

in eight progressively increasing doses to a total amount of 40,000 units, and the abscess was irrigated through the cervical opening with a mixture of staphylococcus and streptococcus bacteriophages. No more serum was given, but the irrigations with bacteriophage were continued. There was gradual improvement. However, on December 3 roentgen examination disclosed a pleural exudate, and on December 4 a thoracentesis yielded 750 cc. of thin fluid containing hemolytic streptococci. A second thoracentesis, on December 10, yielded 15 cc. of yellow fluid. On December 12 the patient was out of bed. The wound in the neck was healing, and he was discharged on December 16 in good condition. The result in this case was unexpectedly gratifying. In October 1935 we heard from him at another hospital, where a diagnosis of lymphosarcoma had been made.

Case 50.—J. B., a woman aged 80, was admitted to the hospital on Jan. 4, 1935, with a "running ear" which had opened spontaneously on Nov. 26, 1934. On Jan. 6, 1935, a simple mastoidectomy was performed on the left, and pus containing hemolytic streptococci was found. After the operation the temperature rose, reaching 103.8 F. on January 7 and 106 F. on January 9. A culture of blood taken on January 9 remained sterile. On the same day the spinal fluid contained 2,500 cells per cubic millimeter, and streptococci were visible on direct microscopic examination. Two days later, on January 11, concentrated streptococcus serum (New York state) was given in divided doses to a total of 10,000 units. A rather severe reaction to the serum required the injection of epinephrine. On January 12 she received 8,000 units, and on January 13, an intramuscular injection of 10,000 units and 10,000 units intravenously. This was followed by trembling of the entire body and moderate cyanosis. On the afternoon of this day she lapsed into coma, and she died at 2:40 a. m. January 14. Necropsy revealed purulent cerebrospinal meningitis. The total amount of serum used was 38,000 units.

Case 52.—J. Z., a boy aged 1 year, was admitted to the hospital Jan. 10, 1935, with a temperature of 103.2 F. He had been ill with rhinitis since December 26 and with pneumonia since December 28. On January 10 a bilateral myringotomy was performed. On January 11 a culture of the blood was made, which gave a growth of hemolytic streptococci. The temperature had reached 104.6 F. On January 12 an abscess on the anterior aspect of the right forearm was incised; it yielded 30 cc. of thick green pus. A similar abscess in the occipital region was incised, and 10 cc. of pus was obtained from it. Both specimens contained streptococci. A transfusion of 250 cc. was given, and 40,000 units of concentrated streptococcus serum (New York state) was administered intramuscularly. On January 13 the patient was given additional serum (40,000 units) intravenously. A culture of blood taken on this day remained sterile. On January 14 a transfusion of 100 cc. was given, and on January 15, another intravenous dose of 40,000 units of concentrated serum. A blood culture made on this day remained sterile. On January 16 myringotomy and simple mastoidectomy were done on the left. The pus found during these operations yielded pneumococci. The temperature continued to range between 100.8 and 102.4 F. On January 18 roentgen examination revealed distention of the left hip joint with separation of the head of the femur. Serum rash appeared on January 20. On January 23 the left hip was opened, and 20 cc. of pus was obtained. A culture of this pus yielded Str. haemolyticus. From January 31 to February 5 the temperature remained below 99 F., but on February 5 it ascended to 103.4 F. and continued to spike daily until February 23. Cultures of blood taken February 11 and February 21 remained sterile. A roentgenogram taken on February 18 revealed destructive osteomyelitis

of the hip. On March 28 the incision of the femur and hip was extended to promote drainage. Culture of the exudate yielded hemolytic streptococci. A culture of blood taken April 1 remained sterile. After April 20 the temperature remained normal, and the patient was discharged with a draining sinus on April 23. The total amount of concentrated serum used was 120,000 units, and of blood given by transfusion, 1,100 cc. When serum therapy was discontinued culture of the blood was already sterile and the child's life seemed secure, but perhaps if we had persisted longer in the administration of the serum the patient might have been spared some of the serious complications.

Case 53.—R. N., a man aged 62, was admitted to the hospital Feb. 8, 1935, with an ear which had been discharging since Dec. 8, 1934. Simple mastoidectomy on the left side was done on February 8, and culture of material from the mastoid yielded hemolytic streptococci. On February 10 the patient had a chill, and culture of blood taken on February 11 yielded twelve colonies of streptococci per cubic centimeter of blood. On February 12 the jugular vein was ligated on the left and the mastoid wound was reopened. On February 13 a transfusion of 500 cc. was given. On February 14 respirations were rapid; there was evidence of pneumonia and the left knee was painful. On February 15 a transfusion of 250 cc. of blood was given. The temperature was 105 F. A culture of blood taken on this day again showed hemolytic streptococci. On this date concentrated streptococcus serum was given, 20,000 units intravenously. Culture of blood taken on February 16 yielded more than 400 colonies per cubic centimeter of blood. On this day the patient was given 20,000 units of serum intravenously. On February 17 he was given 40,000 units of serum intravenously. Death occurred at 9 a. m., February 17. The total amount of serum used was 100,000 units. Early administration of the serum would seem to promise better results in such a case.

Case 55.—R. A., a boy aged 13 months, was admitted to the hospital Feb. 16, 1935, with pharyngitis and an abscess in the left anterior cervical region, which had been present for two weeks. Incision of the abscess on February 18 released pus containing hemolytic streptococci. The temperature had remained between 102 and 103.8 F. but rose to 104 F. on February 25 and February 28. A culture of blood taken on March 1 gave a positive growth of the same type of streptococci. Subsequent cultures, made on March 3, 4, 5, 7, 9 and 13, produced the same organism, but the one taken on March 18 remained sterile. The child's temperature fell to normal and did not exceed 100 F. after March 11, so that the fact that a culture of blood taken on March 13 yielded bacteria is rather remarkable. Unconcentrated streptococcus serum (New York state) was administered, 10,000 units intravenously on March 2, and on March 3 the concentrated serum 20,000 units intravenously, was given. The same dose was administered on March 4, 40,000 units on March 5 and 20,000 units each on March 6, 7 and 8, when serum was discontinued. Serum rash appeared on March 10 and became generalized on March 11. Then the temperature fell to normal. The child was discharged in good condition on March 20. The total amount of serum used was 170,000 units.

Case 56.—M. B., a boy aged 6 years, was admitted to a hospital in Westchester County, N. Y., on Feb. 27, 1935, with acute otitis media on the right and a temperature of 104 F. Myringotomy was performed on February 27 and mastoidectomy March 4. A culture of blood, taken on March 4, yielded hemolytic streptococci, and the infection of the blood stream persisted until death. Twelve transfusions were given at intervals of four days. Concentrated streptococcus serum (New York state) was given on March 4, 5, 7, 8, 10 and 14, to a total of 140,000 units.

Serum was discontinued after March 14. About two weeks later bronchopneumonia with multiple abscesses of the lung was recognized, and the child died on April 5.

CASE 61.—J. G., a girl aged 4 months, was admitted to the hospital March 30, 1935, with fluctuating swelling of the right cervical and the upper thoracic region, complicating an infection of the upper part of the respiratory tract, of two weeks' duration. The swelling was incised, and a large amount of pus was released on the day of admission. Culture of the pus yielded Staphylococcus aureus. Bilateral myringotomy was done on April 3, and this bilateral operation was repeated on April 12. On the next day the temperature reached 104.4 F. A culture of blood taken on this day remained sterile. On April 19 there was generalized erythema, and the temperature ranged between 100 and 101 F. On April 25 the temperature rose to 103.6 F., and on April 26 bilateral simple mastoidectomy was performed. Exudate from both mastoids yielded cultures of hemolytic streptococci. On the next day, April 27, the temperature reached 104 F. A culture of the blood was made, and this yielded a growth of hemolytic streptococci. On April 29 spinal tap yielded normal fluid, and culture of blood taken on this day remained sterile. The following night the temperature rose to 105 F., and culture of blood taken on April 30 gave a positive growth of hemolytic streptococci. Concentrated streptococcus serum (New York state) was given, 20,000 units in divided doses on April 29, by intracutaneous, subcutaneous, intramuscular and intravenous routes; 20,000 units intravenously on each of the next three days, April 30, May 1 and May 2; on May 3, an intravenous injection of 15,000 units, and on May 4, 5,000 units subcutaneously. The child improved rapidly. Cultures of blood taken on May 1 and May 2 remained sterile, and the patient was discharged in good condition on May 7. The total amount of serum used was 100,000 units.

CASE 62.—W. F., a boy aged 5 months, was admitted to the hospital on April 30, 1935, with purulent rhinitis and redness and swelling of the face, the neck and the upper part of the thorax, diagnosed as erysipelas. On May 1, erysipelas antitoxin (Squibb) was injected intramuscularly in divided doses to a total amount of 10.5 cc., and this dose was repeated on May 2. A culture of blood taken on May 2 gave a positive growth of hemolytic streptococci. On May 3 a transfusion of 150 cc. was given by the Unger method. The child was treated with ultraviolet rays for two minutes and was given 10,000 units of concentrated streptococcus serum (New York state) on May 3 and again on May 4. On May 5 there was evidence of bronchopneumonia. Concentrated streptococcus serum (New York state), 20,000 units, was given by intramuscular injection. A culture of blood taken on this day remained sterile, and the clinical condition seemed more satisfactory. On May 6, an intravenous injection of 5,000 units of unconcentrated streptococcus serum (New York state) was given, and this dose was repeated on May 7. The child died on May 8. Permission for necropsy was not obtained.

CASE 65.—L. S., a boy aged 5 years, was admitted to the hospital May 8, 1935, with a temperature of 105 F., a stiff neck and earache present since May 5. Bilateral myringotomy was performed on May 8, and on May 9 a spinal tap yielded normal fluid. Culture of blood taken on this day yielded two colonies per cubic centimeter of blood. On May 10 both ear drums were again incised. On May 11 the growth in the culture made on May 9 was recognized. At clinical consultation it was evident that the child had bilateral otitis with severe mastoiditis, metastatic abscess on the dorsum of each hand, rapid pulse and a dilated heart without recognizable murmur. The possibility of vegetative endocarditis

was given serious consideration, and the otologist felt that the child was not in good condition for a mastoidectomy and recommended that operation be deferred. Serum therapy was therefore requested and was instituted on May 11. An intracutaneous injection of 0.05 cc. of concentrated streptococcus serum (New York state) was given as a test for sensitiveness. The reaction was negative. This test was followed at thirty minute intervals by administration of 1.5 cc. of serum subcutaneously, 3.5 cc. intramuscularly, then 1 cc. intravenously and later 9 cc. intravenously, making a total of 40,000 units in the five doses. A culture of blood taken on this day remained sterile. The swelling on the dorsum of the right hand had increased considerably. On May 12 the child was given a transfusion of 250 cc. at 10:21 a. m. and an intravenous injection of 20,000 units (1 ampule) of con-

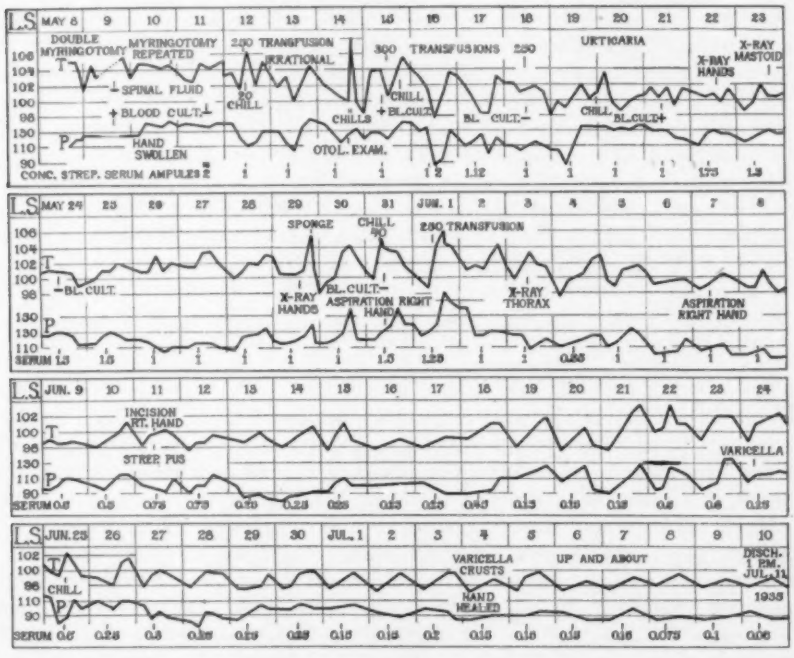

Chart 1 (case 65).—Abridged clinical record of L. S., a boy aged 5 years. The illness began with stiff neck, earache and high temperature. Culture of blood taken on May 9 yielded streptococci. Clinically the child had severe mastoiditis, a metastatic abscess on the dorsum of each hand and a dilated heart. Operation was deferred on account of his bad condition, and serum therapy was instituted May 11. The patient had a stormy course, but the record indicates what may be expected when serum is persistently administered over a long period.

centrated serum at 10:58 a. m. At 11:20 a. m. he had a shaking chill which lasted twenty minutes, with a rise of temperature to 106.2 F. at 12 noon. A culture of blood taken on May 15 yielded streptococci. The dose of serum was increased to three ampules (60,000 units) on May 16. A culture of blood taken on May 18 remained sterile, but culture of that taken on May 21 yielded bacteria. The serum was again increased for four days. On May 22 the record of this patient was presented before the clinical conference, and the general opinion was

discouraging. The sluggish abscesses on the dorsal surface of each hand persisted. Roentgenograms taken on May 22 and on May 29 revealed no evidence of disease of the metacarpal bones. Early in the morning of May 31 the patient had a chill lasting forty minutes. Soon after the chill, a culture of the blood was made (8:48 a. m.), and this remained sterile. At 8:55 a. m. the abscess on the back of the right hand was aspirated, and 3 cc. of thick pus containing streptococci was obtained. This abscess cavity was irrigated with streptococcus bacteriophage. A transfusion of 250 cc. of blood on June 1 was followed by a chilly sensation and a rise of temperature to 106 F., with a pulse rate of 180. On June 2 there were signs of fluid in the left pleural cavity, but roentgenographic examination on June 3 gave negative results, and thoracentesis was not done. The back of the right hand was incised and pus liberated on June 11. The abscess on the back of the left hand resolved without drainage. The dose of serum was decreased for the sake of economy in the period from June 9 to June 21 but was then increased for a few days during the febrile stage of chickenpox, which required segregation of the patient. Serum was then continued in smaller doses until July 11, when the patient was discharged. He was seen from time to time and was readmitted to the hospital on Jan. 20, 1938, with acute purulent otitis media caused by Str. haemolyticus, which has healed rapidly without complications.

Case 68.—M. M., a girl aged 4 years, was admitted to a hospital in New Jersey on June 2, 1935, with a temperature of 106 F. and a history of sore throat since May 18, fever since May 28, abscess on the right side of the neck on May 29 (incised May 31) and myringotomy on the right on June 1. A culture of blood taken on June 2 yielded hemolytic streptococci. On June 3 roentgen examination of the thorax revealed evidence of septic pneumonia. On this day the right ear drum was widely incised. At 1 a. m. on June 4 a transfusion of 250 cc. of blood from an immunized donor was given. On June 5 the temperature was 105.2 F. at 4 a. m., 100 F. at noon and 105 F. at 8 p. m. At 10:30 p. m. concentrated streptococcus serum (New York state), 60,000 units (3 ampules), was given intravenously. The response of the patient was gratifying. The temperature remained low for three days, and cultures of the blood, made on June 7 and again on June 10, remained sterile. The right ear drum was again incised on June 10 to promote better drainage, but the patient slowly lost ground; the high fever returned, and a culture of blood taken on June 16 again revealed infection of the blood stream. Two ampules (40,000 units) of the serum were given on June 17. The patient had a rather severe anaphylactic reaction and was given epinephrine by hypodermic injection and later by intravenous injection. On June 19 another intravenous injection of serum (1 ampule) was followed by a severe reaction. Smaller doses (10,000 units) were given on June 24 and June 26. The right ear drum was again incised on June 28, and on the next day an abscess in the neck was incised. The patient was discharged in good condition on July 3.

This patient was not seen by us, but we were consulted by telephone and letter. It would seem that the continuation of serum therapy for several days early in June might have averted the relapse at the middle of the month. The record indicates a favorable effect of the serum and also illustrates the difficulty encountered in starting serum therapy again after an interval of ten or twelve days.

Case 71.—J. J., a woman aged about 30, the wife of a physician, was seen on Jan. 25, 1936. She had a very red and painful pharynx, mild delirium, a temperature of 104 to 105 F. and a sterile blood culture. Concentrated polyvalent

streptococcus serum (Parke, Davis & Co., biological 2005) was given in divided doses to a total amount of 20 cc. The husband reported a severe shock reaction in the evening. On the morning of January 26 the temperature was normal. Small subcutaneous doses (2 cc.) of the serum were continued. Recovery was prompt, and no relapse occurred.

Case 73.—D. B., a woman aged 22, admitted to the hospital Feb. 7, 1936, with pneumonia, empyema and streptococcus septicemia, has already been discussed in detail in the preceding paper of this series. Her case is an example of successful use of serum therapy in a desperate situation.

Case 74.—E. M., a woman aged 50, got a bone in her throat on Feb. 12, 1936, and at 2 p. m. on February 13, by operation through the esophagoscope, a bone fragment 25 by 15 by 3 mm. was removed. An esophageal wound about 10 mm. in diameter, below the cricopharyngeus muscle on the right side, resulted in pain, dyspnea, cyanosis and crepitation above the clavicles. A superior mediastinotomy was performed on February 13 at 9 p. m., and rupture of the esophagus was

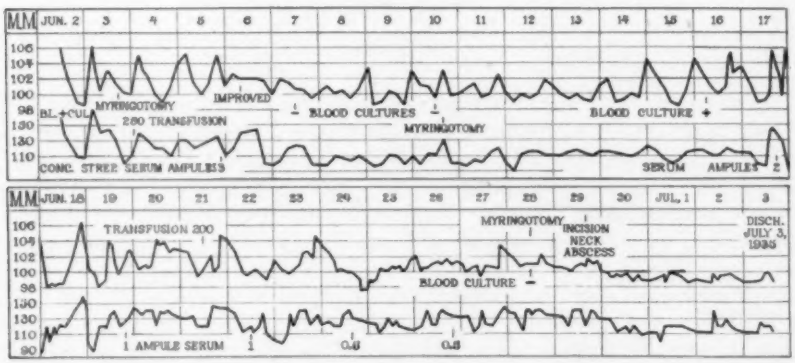

Chart 2 (case 68).—Abridged clinical record of M. M., a girl aged 4 years. This child was admitted to the hospital with a sort throat, otitis media and an abscess on the right side of the neck. Culture of the blood yielded streptococci on the day of admission. She was given a large dose of serum on June 5, to which she responded promptly. Serum was discontinued, however, and the bacteremia returned. On June 17 serum therapy was resumed and continued at forty-eight hour intervals, with a favorable result.

recognized. A feeding tube was passed into the stomach. On February 21 the aid of streptococcus serum was requested by the attending surgeon. Cultures of material from the wound showed predominant hemolytic streptococci. Concentrated polyvalent streptococcus serum (Parke, Davis & Co., biological 2005) was injected into the skin at 11:21 a. m., subcutaneously at 11:26 and 11:41, intramuscularly at 12:12 p. m. and intravenously at 12:42 p. m., 1:39, 2:23, 2:54, and 3:25 p. m., the total amount for the day being 5 cc. of the serum suitably diluted with saline solution for injection. At 4:15 p. m. the patient felt chilly, and the temperature rose to 102.8 F. at 4:30 p. m., falling sharply to 99.4 F. at 12:30 midnight, the lowest temperature since admission. During the next four days there was marked clinical improvement with continued serum therapy, 8 cc. on February 22, 6 cc. on February 23, 6 cc. on February 24, 6 cc. on February 25, 6 cc. on February 26, 4 cc. on February 27, 9 cc. on February 28, 10 cc. on February 29, 10 cc. on March 1,

10 cc. on March 2 and 6 cc. on March 3. The clinical improvement from February 21 to February 25 was followed by a period of unsatisfactory behavior. The temperature rose to 103 F. on February 25. A generalized serum rash appeared on February 29. The temperature reached 104 F. on this day and 104.6 F. on March 1 and March 2. On March 3 an intravenous injection of 4 cc. of serum diluted with 6 cc. of saline solution was given at 9:30 a. m. Five minutes later the patient had a "convulsion" lasting two minutes, during which the pulse was imperceptible. This was followed by a chill which lasted fifty minutes, with a rise in temperature to 106.2 F. at 11:05 a. m. At 11:47 a. m. another intravenous injection of 2 cc. of serum diluted with 8 cc. of saline solution was given, without reaction. Serum therapy was then discontinued. At 4 a. m. on March 4 the temperature was 98. The patient was finally discharged from the hospital on March 27, in good condition.

Case 75.—H. T., a boy aged 14, was admitted to the hospital March 12, 1936, with a temperature of 101.6 F. He had been ill with "tonsillitis and influenza" for two weeks. Roentgen examination at 11 a. m. on March 13 revealed free fluid in the left thoracic cavity, and at 5 p. m. thoracentesis yielded 750 cc. of straw-colored fluid in which hemolytic streptococci were found in pure culture. Examination for tubercle bacilli, including inoculation of a guinea pig, gave negative results. On March 18, streptococcus serum (Parke, Davis & Co., biological 2005) was given, 0.05 cc. of a 1:10 dilution into skin at 1:21 p. m., 1 cc. of a 1:10 dilution subcutaneously at 1:30 p. m., 4 cc. of a 1:10 dilution into muscle at 2:48 p. m. and 10 cc. of a 50 per cent dilution into muscle at 4:55 p. m. The serum was given intravenously on March 19, at 10:42 a. m., 5 cc. of a 1:20 dilution; at 1:48 p. m., 5 cc. of a 1:5 dilution; and at 3:20 p. m., 2 cc. of serum diluted with 3 cc. of saline solution. This patient was not in an alarming condition. The dose of serum was slowly increased to 20 cc. per day, and on March 25, at the onset of serum sickness, the amount of serum was decreased to that which the patient could tolerate, namely 1 cc. of serum per day in three intravenous doses. The dose was reduced to 0.5 cc. per day as the patient improved, and this was continued until his discharge on May 31. Thoracotomy with removal of 5 cm. of the ninth rib was performed on March 31, and on April 28 about 5 cm. of the eighth rib was resected. The total amount of serum used was 157.85 cc. from March 18 to May 31.

After a vacation in the country, this boy returned on August 27 for a tonsillectomy, which was not followed by any complication.

Case 76.—T. L., a woman aged 33, with chronic pulmonary tuberculosis whose sputum contained acid-fast bacilli, had been treated surgically. Pneumothorax was established in June 1935; subsequently pleural adhesions on the left side were severed in December 1935 and again in January 1936. On February 28 thoracotomy was performed. The thin pus obtained yielded a pure culture of hemolytic streptococci. On March 18 the patient was irrational and required oxygen to relieve dyspnea and cyanosis. The temperature reached 104.6 F. The attending physician requested bacteriotherapeutic aid to combat the streptococcus. A culture of blood taken on this date remained sterile. The chest fluid now contained a few gram-negative bacilli in addition to the hemolytic streptococci. Streptococcus serum (Parke, Davis & Co., biological 2005) was given by intracutaneous, subcutaneous, intramuscular and intravenous injection to a total amount of 1.2 cc. on March 18. The divided doses of serum were continued by intravenous injection, 3.5 cc. of serum on March 19, 8 cc. on March 20, 10 cc. on March 21, 22 and 23, 20 cc. on March 24, 10 cc. on March 25 and 26 and 5 cc. on March 27. The purulent exudate

from the pleural cavity now contained relatively few streptococci and abundant gram-negative bacilli. Serum therapy was discontinued. On March 27 an intercostal thoracotomy in the seventh intercostal space at the anterior axillary line was performed, and a drainage tube was inserted in this region. The patient gradually gained in strength and was discharged on July 12, with a persistent sinus. Although she was able to be up and about, the prognosis was unfavorable.

CASE 78.—W. H., a man aged 43, was brought to the hospital by ambulance on March 31, 1936. He had been suffering from a head cold since March 3, otitis media on the right with spontaneous rupture of the ear drum on March 24, moderate fever and swollen, painful joints. A culture of blood taken on March 31 remained sterile. On April 1 the opening in the right ear drum was enlarged by incision. The swelling about the joints continued to increase, and on April 3 both forearms and the left ankle were thought to be purulent. At 5:40 p. m. on April 3, incision of the left ankle and left forearm released purulent exudate in which chains of streptococci were evident on direct microscopic examination. The cultures yielded pure growth of hemolytic streptococci. Without waiting for the result of the culture, serum therapy was started at 6:45 p. m. by intracutaneous, then subcutaneous, then intramuscular and finally intravenous injection, a total of 8.7 cc. of streptococcus serum (Parke, Davis & Co., biological 2005) being used from 6:45 to 8:40 p. m. On April 4 the patient seemed somewhat better. The serum was continued in repeated doses at intervals of twenty to sixty minutes from 9:34 a. m. to 4:20 p. m., the total amount of serum being 23 cc. At 4:55 p. m. the patient had a severe chill lasting thirty minutes, with a rise of temperature to 107.6 F. at 5:35 p. m. There was then profuse diaphoresis which continued until midnight, and the temperature fell to 96.2 F. at 4 a. m. This appears to have been a typical bacteriotherapeutic shock, which we have in the preceding paper designated as the Hugh Young reaction. Intravenous injections of serum were continued every day until the patient was discharged from the hospital on May 16, and he returned for further injections on May 18 and 19. On May 19 he was finally dismissed. Pyemic abscesses in the left thigh, the right leg and the right forearm were incised on April 10. The two cultures of the blood, one made on March 31 and one on April 4, remained sterile. The total amount of serum used was 150.7 cc.

CASE 79.—W. B., a boy aged 8, suffered an attack of measles in March 1936, followed by otitis media and discharge from the left ear since April 5. He was admitted to the hospital on April 17, and mastoidectomy on the left was performed on this day. Culture of material from the mastoid exudate gave a pure growth of hemolytic streptococci. The postoperative progress was unsatisfactory. A transfusion of 350 cc. of blood was given on April 26, and a culture of blood taken on this day remained sterile. On April 27 there was a questionable chill, and the temperature rose to 105.2 F. at 7 p. m. At 7:30 p. m. the left internal jugular vein was ligated, and a clot was removed from the left lateral sinus and jugular bulb. On April 29 there was again a slight chill at 11:40 a. m. Blood was taken for culture, and a transfusion of 250 cc. was given. This was followed by a severe chill lasting twenty-five minutes, with a rise of temperature to 106 F. On the following morning the growth of streptococci was evident in the blood culture of April 29. On April 30 serum therapy was begun with the intracutaneous injection at 9:27 a. m. of serum (Parke, Davis & Co., biological 2005) followed by two subcutaneous injections at intervals of fifteen minutes, two intramuscular injections and four intravenous injections of the same serum, the last one at 11:57 a. m. The total amount of this serum used was 2 cc., and half of this was

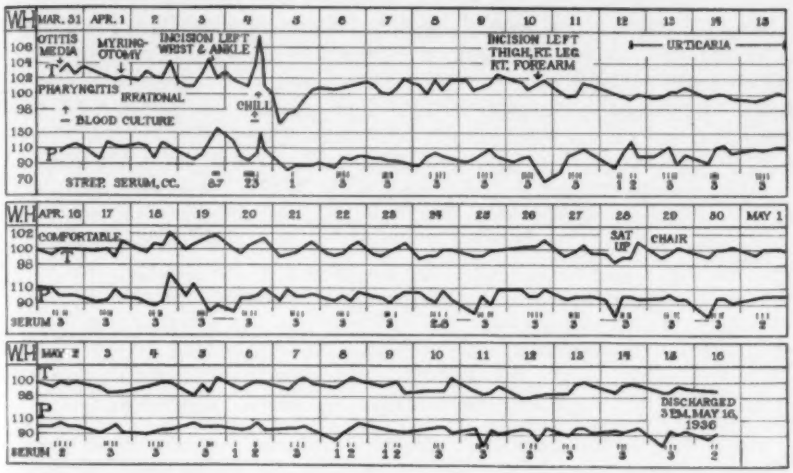

Chart 3 (case 78).—Abridged clinical record of W. H., a man aged 43. In this patient, swollen, painful joints and otitis media with spontaneous rupture of the ear drum had followed a persistent head cold. After pus from the ankle and wrist revealed streptococci, serum therapy was started on April 3. This was continued on April 4, at frequent intervals, to a total of 23 cc., culminating in that typical bacteriotherapeutic shock which we have designated as the Hugh Young Reaction. Serum was continued daily until the patient's discharge, which took place after a fairly uneventful convalescence.

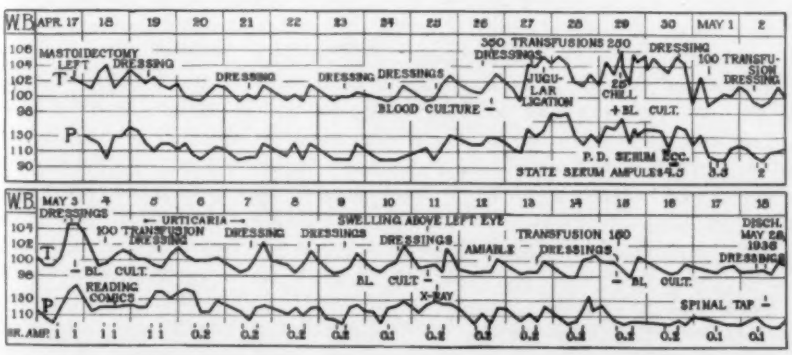

Chart 4 (case 79).—Abridged clinical record of W. B., a boy aged 8. This boy had bacteremia following mastoidectomy and ligation of the left internal jugular vein with the removal of a clot from the left lateral sinus and jugular bulb. Administration of serum on April 30 was followed by prompt improvement. On May 3 the temperature again rose, and there was severe headache. The amount of serum was reduced to one tenth of the previous dose on May 6, and small daily doses were continued through May 18. He was discharged on May 28; complete recovery ensued.

administered by the intravenous route. Beginning at 12:17 p. m. unconcentrated streptococcus serum of the New York state department of health was given intravenously in nine spaced injections, the first one 0.2 cc. and the last one 10.5 cc. at 3:37 p. m., the total amount of this serum being 17.5 cc., or 22,500 units. At 4 p. m. the patient's temperature was 105.2 F. At 5:50 p. m. the wounds were dressed with the patient under nitrogen monoxide oxygen anesthesia administered for fifteen minutes. The patient slept fairly well and perspired freely during the night, and clinical improvement was evident on May 1 and 2. On May 3, however, there was severe headache. A culture of blood taken on this day remained sterile. Subsequently the patient continued to improve slowly, although frequent headaches, paresis of the left facial muscles, a tendency to left internal squint and edema above the left eye suggested continuing inflammatory activity within the cranium. Urticaria of moderate severity was present from May 5 to May 7, and the dose of serum was reduced to one tenth of the previous amount on May 6. Serum therapy was terminated on May 18, and the patient was discharged from the hospital on May 28. Complete recovery followed.

Case 80.—A. S., a woman aged 45, was admitted to the hospital on April 20, 1936, and on April 24 underwent a partial gastrectomy for diffuse scirrhous carcinoma of the stomach, which could not be completely removed. Four days later pneumonia of the left lung was recognized. As the patient improved from this, severe pharyngitis developed, and on May 4 there was a definite chill. Bacteriologic examination revealed abundant hemolytic streptococci in the throat. Streptococcus serum (Parke, Davis & Co., biological 2005) was injected in small doses from May 6 to May 20, the total amount being 14.54 cc. The pharyngitis was much improved by May 14. The patient was out of bed daily after May 15. She was discharged from the hospital on June 30, in apparently good condition.

Case 81.—J. W., a man aged 44, was admitted to the hospital April 28, 1936, with chronic nasal sinusitis, acute sore throat and swollen jaw. The abscess of the jaw and a peritonsillar abscess were incised and drained on May 6. At 11:20 a. m. on May 15 the patient had a chill which lasted thirty minutes, and his temperature, which had been below 100 F., rose to 102.2 F. He complained of dyspnea and vomited a large amount of undigested food. A culture of blood taken at this time remained sterile. Spinal tap yielded cloudy fluid containing pus cells and streptococci seen in direct microscopic examination. At 12 midnight mastoidectomy was performed, and on the next day the aid of bacteriotherapeutic measures was urgently requested. Multiple injections of streptococcus serum were given from 12:38 to 3:48 p. m., the total amount being 30 cc. The patient had a severe chill at 4 p. m. which lasted thirty minutes, with a rise in temperature to 106 F. At 6:30 p. m. spinal tap yielded 60 cc. of cloudy fluid, and 20 cc. of the serum was injected into the spinal canal. At 1 a. m. administration of oxygen was started and continued. The patient died at 4 a. m.

Case 85.—G. P., a man aged 32, a surgeon, was admitted to the hospital at 3:20 a. m., Jan. 12, 1937, with acute maxillary sinusitis complicating a head cold of one week's duration. The patient appeared very toxic. The maxillary sinus was punctured on the morning of January 12. The exudate contained abundant hemolytic streptococci. Sulfanilamide in doses of 20 grains (4 tablets) every six hours was started about 6 p. m. on January 13. At 8 p. m. he was given 1 ounce (30 cc.) of whisky; at 9 p. m. a hypodermic injection of ⅙ grain (0.01 Gm.) of morphine, and at 9:30 ¼ grain (0.015 Gm.) of codeine by mouth. He slept for about two hours. At 12:15 1½ grains of phenobarbital was given, as well

as 30 grains of triple bromides and at 12:45 an eggnog containing ½ ounce of whisky. He was given 20 grains (1.29 Gm.) of sulfanilamide at 1 a. m. At 1:30 a. m. he was sleeping. At 2:35 a. m. (January 14) he awoke in a severe chill which lasted twelve minutes, with a rise in temperature to 102.8 F. After sleeping for another hour he awoke in distress, nauseated, cyanotic and dyspneic. He was also emotionally disturbed. At 4 a. m. the temperature was 104.4 F. The cyanosis became more evident during the forenoon. At a medical consultation at this time it was decided to treat the condition as an infection of the blood stream, and we were requested to see the patient and, after slight delay, to undertake bacteriotherapeutic measures. A culture of the blood was made at 9:40 a. m. on January 14; it remained sterile. Without awaiting the result of this culture the administration of streptococcus serum (Parke, Davis & Co., biological 2005) was begun at 12:25 p. m. by one intracutaneous injection, three subcutaneous injections, three intramuscular injections and two intravenous injections, the last one at 4:42 p. m. The total amount of serum for the day was 5.6 cc. Clinical improvement was evident by midnight. There was marked diaphoresis. At 8:15 a. m. on January 15 the patient awakened smiling. The increasing cyanosis, however, gave considerable concern. The serum was continued by five intravenous injections on January 15 and decreasing amounts thereafter, as shown in the chart. Oxygen administered by funnel on January 15 and 16

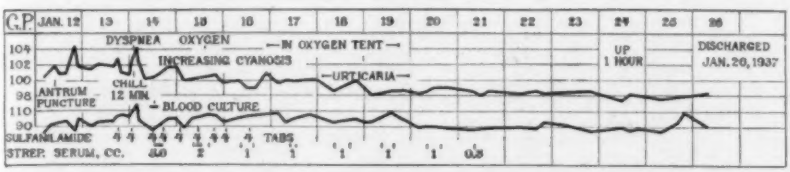

Chart 5 (case 85).—Abridged clinical record of G. P., a man aged 32. This patient had acute maxillary sinusitis. The pus obtained after puncture of the antrum contained abundant hemolytic streptococci. Sulfanilamide (20 grains) was given the evening of January 13, and serum therapy was instituted on January 14. There was marked improvement on January 15. Sulfanilamide was discontinued on January 16 because of severe cyanosis, but serum was continued through January 21. Recovery was prompt.

seemed to produce no change in the patient's color. Spectroscopic examination of the blood at 10 a. m. disclosed the presence of methemoglobin. Sulfanilamide was discontinued, and the patient was placed in an oxygen tent that afternoon. On January 18 there was marked improvement in color, and the oxygen was discontinued on January 19, after which time progress was uneventful. There was mild urticaria on Jan. 18 and 19. Administration of serum was continued until January 21. The surgical point of view in this case and particularly the cyanosis caused by medication have been discussed elsewhere by Stoness.[3]

Case 87.—V. B., a man aged 34, who had been in the hospital under treatment for staphylococcic bacteremia, osteomyelitis of the right ilium and carditis with clinical evidence of lesions of the mitral and aortic valves since Oct. 16, 1936, had a running right ear on Jan. 24, 1937. On February 15 a bacteriologic examination of the exudate disclosed a pure culture of hemolytic streptococci. The

3. Stoness, J. F.: Methemoglobinemia and Prontylin, New York State J. Med. **37**:1139-1140 (June 15) 1937.

patient was given sulfanilamide, 5 grains (0.32 Gm.) on February 16, before mastoidectomy, and 5 grains three times a day from February 17 to 25. We also gave him streptococcus serum (Parke, Davis & Co., biological 2005) as follows: 3.25 cc. on February 16, 2 cc. on February 17, 1.4 cc. on February 18, 1 cc. daily from February 19 to February 26 inclusive and 0.5 cc. on February 27 and 28. Mastoidectomy on February 16 was followed by rapid healing of the wound, so that local irrigations were discontinued on March 4 and no further attention to the ear was required. There was a mild serum rash on February 27 and 28. The streptococcic otitis media was merely a minor incident in the prolonged illness of the patient. Part of his clinical record has already been published.[4] He was eventually discharged from the hospital on November 12 and has remained in good condition since.

Case 88.—E. R., a woman aged 28, attempted to remove wax from the left auditory canal by use of a toothpick on Feb. 17, 1937, and in the evening she noticed two small swellings behind the ear and one in front of the ear. On the next day the swelling extended rapidly to involve the left half of the face. She was admitted to the hospital at 1 p. m. on February 20, at which time the swelling extended from the left mastoid region to the left side of the nose. There was marked edema of the left lower eyelid and of the cheek, particularly about the

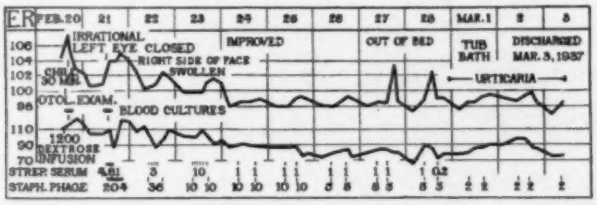

Chart 6 (case 88).—Abridged clinical record of E. R., a woman aged 28. This patient was admitted to the hospital on February 20 with swelling of the left half of the face, extending from the mastoid region to the nose. Edema of the left lower eyelid was noticed. The temperature rose to 107.4 F. after a chill which occurred the same afternoon. Bacteriologic diagnosis was not waited for; the patient was treated for both streptococcus and staphylococcus infections, being given streptococcus serum (Parke, Davis & Company) and also staphylococcus bacteriophage. These agents were both continued as indicated on the chart. Recovery was prompt and uneventful.

opening of Stenson's duct. The temperature was 104.4 F.; the leukocyte count was 18,300, with 95 per cent polymorphonuclears. An intravenous infusion of 1,200 cc. of 5 per cent dextrose solution was given. The results of otologic examination by Dr. Griffith were recorded as follows: "Cellulitis involving auricle with surrounding tissue; middle ear and mastoid normal." Immediately after this the patient had a severe chill lasting from 4:15 to 4:45 p. m., with a rise of temperature to 107.4. Culture of blood taken during the chill remained sterile. On the next day, February 21, the facial swelling had extended to involve the left upper eyelid and forehead, so that the left eye could be opened with difficulty, and had extended to the right side of the face. Marked edema was present about the right eye. The eyeballs appeared normal. Bacteriotherapeutic aid was requested

4. MacNeal, W. J.: The Infectious Organism in Osteomyelitis, J. Bone & Joint Surg. **19**:889-891 (Oct.) 1937.

by the attending surgeon. In the absence of a specific bacteriologic diagnosis it was decided to treat the patient for both streptococcic and staphylococcic infection without further delay. Streptococcus serum (Parke, Davis & Co., biological 2005) was given in divided doses, beginning at 12:10 p. m. by intracutaneous injection, followed by four subcutaneous injections and two intramuscular injections. The last injection was given at 3:40 p. m. The total amount of serum used was 4.61 cc. Staphylococcus bacteriophage was given intravenously in a series of fourteen injections, beginning with 1 cc. at 12:11 p. m. and ending with a dose of 35 cc. at 9:15 p. m., the total amount of bacteriophage being 204 cc. At 6 p. m. the temperature reached 105 F., and the patient complained of feeling cold. There was, however, no frank chill, and at 7:55 p. m. the temperature was still 105 F., falling to 104.6 at 10 p. m. and to 103 at 4 a. m. on February 22. The serum was continued in increasing amount on February 23 and then in small doses to February 28. The bacteriophage was continued in decreasing doses daily to March 3, when the patient was discharged. She has returned twice for immunizing injections and appears to have made a complete recovery. The diagnosis remains somewhat unsatisfactory, but the dissatisfaction in this respect is somewhat ameliorated by the prompt recovery of the patient from an apparently serious disorder.

Case 89.—K. C., a woman aged 40, admitted to the hospital on April 15, 1937, is one of the most remarkable patients in this entire series. Her record has been reported elsewhere.[5] Here it will suffice to say that the patient received sulfanilamide literally ad nauseam, streptococcus serum in large amounts for eight days and in smaller amounts for thirty-four days more, and streptococcus bacteriophage beginning on the thirteenth day of hospitalization and continuing for thirty-three days. She was discharged in good condition on May 29. She has reported from time to time and was seen again on Feb. 3, 1938, at which time she was in excellent physical condition.

Case 90.—B. D., a man aged 42, was admitted to the hospital on May 17, 1937, by transfer from another hospital. He had streptococcic bacteremia, apparently originating in otitis media early in April, with complicating pneumonia, pleurisy and suspected endocarditis. He was treated with large amounts of sulfanilamide and streptococcus serum. He died June 13, and necropsy was not permitted. The record of this case has been presented in the preceding paper of this series.

COMMENT

In this series of 30 patients there were 7 deaths. Generalized meningitis with streptococci recognizable in the spinal fluid was present before serum therapy was initiated in 3 of the cases in which fatality occurred, namely cases 33, 50 and 62. We have no evidence to indicate that established diffuse streptococcic meningitis can be controlled by the serum which we have employed. In only 1 instance (case 39), the patient being a boy aged 10 years, was there recovery after definite evidence of meningitis, and in this case, although the spinal fluid was

5. MacNeal, W. J., and Cavallo, M. E.: Streptococcic Bacteremia and Apparent Thrombosis of the Cavernous Sinuses with Recovery, J. A. M. A. **109**: 2139-2141 (Dec. 25) 1937.

clouded with abundant leukocytes, culture failed to disclose the presence of streptococci in it. The other 4 deaths occurred in patients with streptococcic bacteremia but without meningitis. For the patient in case 53 the serum was used late. The patient in case 56 was given 140,000 units of the concentrated serum (New York state) from March 4 to 14, and then serum therapy was discontinued. Two weeks later bronchopneumonia was recognized; the condition ended in death on April 5. The patient in case 62, aged 5 months, received the concentrated serum (New York state) on May 3, 4 and 5, when a sterile culture of blood was obtained. Smaller doses of unconcentrated serum (New York state) were then given on May 6 and 7. Death occurred on May 8. In this case there seems to have been a frank failure after reasonable use of the serum. The patient in case 90, a man aged 42, was treated with sulfanilamide until May 17 for streptococcic bacteremia originating from otitis media early in April. Streptococcus serum was used from May 17 until death of the patient on June 13. This also is an instance of frank failure of serum therapy after reasonable use. It would be only fair to say that the serum therapy was begun rather late and that there was some indication of vegetative endocarditis which cannot be recorded with confidence in the absence of necropsy.

Among the 23 cases in which the patients survived there were 2 examples of streptococcic otitis media developing in debilitated patients under treatment for staphylococcic osteomyelitis (cases 34 and 87). One of the patients received serum, and the other received serum and sulfanilamide. With both the streptococcic infection proved to be only a minor incident. There were 2 patients with mediastinitis and 1 with streptococcic empyema following pneumothorax for active pulmonary tuberculosis. In all 3 of these the activity of the streptococcus, which threatened to be terminal, was adequately controlled. Two patients had streptococcic pneumonia complicated by voluminous empyema (the patients in cases 73 and 75). One of these, the patient in case 73, responded in an unexpectedly fortunate way, and the other made a good recovery. The patient in case 89, whose case is reported in more detail elsewhere,[5] presented the classic symptoms and signs of septic thrombosis of the cavernous sinuses in the presence of a positive infection of the blood stream with hemolytic streptococci. Sulfanilamide, serum and bacteriophage all were brought into play in this case, with a successful outcome apparently unique in the records. In case 68 the immediate improvement after the first day of serum therapy was so gratifying that the serum was discontinued. Relapse required further serum for its eventual control.

The difficulties and dangers in the use of streptococcus serum are serious and require frequent mention. In a subsequent paper in this

series we hope to consider these in more detail. They are such as to require considerable attention and effort on the part of the physician. On this account we recognize that streptococcus serum will not and probably should not be used for streptococcic infections of moderate severity, which may be adequately controlled by the oral administration of sulfanilamide. When, however, a really grave situation arises in a case of streptococcic infection the proper use of the serum brings a promise of important aid which should not be neglected. Certainly in the all too frequent streptococcic infections of the nose, throat, ear and mastoid the use of sulfanilamide or of serum or of the two in combination may be expected to control the infection and to obviate the necessity of operative procedures. For example, mastoidectomies for streptococcic infection, which formerly constituted about 90 per cent of mastoid operations, will become less frequent when modern chemotherapy and serum therapy for streptococcic infections of the upper part of the respiratory tract and of the middle ear are adequately employed. The success already achieved promises even more for the future development of chemotherapy and specific biotherapy of these infections.

SUMMARY

Thirty patients suffering from severe infection with hemolytic streptococci in the field of otolaryngology, 4 with complicating meningitis and 15 whose blood yielded bacteria on culture, were treated with streptococcus serum of three different kinds, together with other therapeutic measures, including transfusions, sulfanilamide and bacteriophage in certain instances. Seven deaths and 23 survivals occurred.

The early use of serum may be expected to be almost always successful, but because of the effort and expense involved serum therapy will usually be reserved for the more difficult cases.

Advanced and even desperate streptococcic infections may be favorably influenced by the adequate use of streptococcic serum.

The timely exhibition of modern chemotherapeutic and biologic agents for the control of infection with hemolytic streptococci may be expected to reduce appreciably the need for operative procedures for control of such infection and, even after surgical incision, to contribute essentially to reduction of the postoperative mortality and period of convalescence.

SQUAMOUS CELL CARCINOMA OF THE RENAL PELVIS

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The occurrence of epithelial tumors of the renal pelvis is rare in comparison with the frequent occurrence of other neoplasms involving the kidney. Joly [1] in reviewing a collected series of 337 cases of tumor of the renal pelvis reported the occurrence of 120 benign papillomas, 138 papillary carcinomas, 29 transitional cell carcinomas and 50 squamous cell carcinomas. In analyzing individual cases it is difficult to classify the tumor accurately, because a varied terminology has been used, as is illustrated by the collected series of nonpapillary tumors of the renal pelvis which Kretschmer [2] studied in 1917. I found that the following terminology had been employed by various authors cited in his collected series. Medullary carcinoma was used by 4 authors; scirrhous carcinoma by 2; pavement epithelium carcinoma by 3; alveolar carcinoma by 3; carcinomatous growth by 2; carcinomatous degeneration by 2; cancer by 3; pavement epithelioma by 9; encephaloid carcinoma by 2; epithelioma by 2; cylindric epithelioma by 1; adenocarcinoma by 1; epidermoid carcinoma by 1; cylindric cell carcinoma by 2; squamous epithelioma by 1; carcinoma-sarcoma by 1, and squamous cell epithelioma by 1. Two authors did not classify the tumor. In some instances a complete microscopic report was not cited, so that correct grouping is impossible.

In 1934, Gilbert and MacMillan [3] reviewed the literature and compiled 55 cases of squamous cell carcinoma of the renal pelvis. They added 2 of their own. Silverstone [4] and Nicholson [5] each reported a

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From the Cleveland Clinic.

1. Swift-Joly, J.: Tumors of the Renal Pelvis and Ureter, Brit. J. Urol. **5**: 327-328 (Dec.) 1933.

2. Kretschmer, H. L.: Primary Non-Papillary Carcinoma of the Renal Pelvis, J. Urol. **1**:405-437 (Aug.) 1917.

3. Gilbert, J. B., and MacMillan, S. F.: Squamous Cell Carcinoma of the Renal Pelvis with Special Reference to Etiology, Ann. Surg. **100**:429-444 (Sept.) 1934.

4. Silverstone, M.: Squamous Cell Carcinoma of the Renal Pelvis: Report of a Case, Brit. J. Surg. **24**:332-336 (Oct.) 1935.

5. Nicholson, W. F.: Squamous Cell Carcinoma of the Renal Pelvis in a Horseshoe Kidney, Brit. J. Surg. **23**:397-399 (Oct.) 1936.

case in the following two years, bringing the total to 59. Five patients with squamous cell carcinoma of the renal pelvis have been seen at the Cleveland Clinic. Including these cases, then, the literature now contains 64 reports of squamous cell carcinoma of the renal pelvis.

REPORT OF CASES

CASE 1.—A woman 41 years of age entered the clinic on Aug. 10, 1924. She complained that for one month she had had chills, fever, profuse sweats and occasional hematuria. Four years prior to this time, three stones had been removed from the left kidney, and one year previously a mass had been discovered in the right side. This had grown rapidly and had become increasingly tender. At the beginning of the onset of the most recent symptoms, two small calculi, which apparently came from the right kidney, had been passed.

Physical Examination.—Physical examination revealed a large mass in the region of the right kidney. It was fixed to the adjacent structures and was tender on palpation.

Laboratory Data.—Examination of the urine showed it to have a specific gravity of 1.006. Its reaction was alkaline; there was a faint trace of albumin, but no sugar was present. Microscopically, red blood cells were numerous, and there were 40 or 50 white blood cells per high power field. Examination of the blood revealed 3,000,000 red cells and 22,000 white cells per cubic millimeter, with 65 per cent of hemoglobin. The value for urea was 29 mg., and that for sugar 98 mg., per hundred cubic centimeters of blood. When the renal function was tested with phenolsulfonphthalein there was excretion of 20 per cent at the end of the first hour and of 25 per cent at the end of the second hour, a total of 45 per cent.

A roentgenogram of the kidneys, the ureters and the bladder showed the outline of the right kidney to be very large, extending well out and below the crest of the ilium.

Cystoscopic Examination.—The urine in the bladder was found to be cloudy. Except for the region around the right ureteral orifice the bladder appeared normal. In this region there was a nodular "cauliflower" growth the size of a small walnut, and the ureteral orifice could not be identified. A catheter was passed to the pelvis of the left kidney, and a test of function was made with phenolsulfonphthalein. The dye appeared from the left kidney in three minutes, and the excretion at the end of one-half hour was 36 per cent. Ten per cent was collected from the bladder.

Diagnosis.—The diagnosis was carcinoma of the bladder, carcinoma of the right kidney and ureter and hydronephrosis.

Operation.—Operation was performed August 18, after a blood transfusion. A great deal of pus was found in the right kidney, and owing to the poor general condition of the patient the kidney was drained. The temperature and pulse rate returned to normal in six days, but chills and fever developed, and the patient died in the hospital twenty-eight days after the operation. Autopsy was limited to examination of the kidney.

Pathologic Examination.—Grossly the specimen consisted of an enlarged right kidney which measured 9 by 5 by 5 inches (22.8 by 12.7 by 12.7 cm.). It was partly firm and was yellowish white, with abundant perirenal fat in which nodules were palpable. The pelvis of the kidney was dilated and was filled with necrotic

material. On section the surface was yellowish red, and toward the central portion it showed degeneration and hemorrhage. The capsule was thickened; it stripped from the kidney with difficulty, showing portions of tumor growth involving the cortex. At the ureteropelvic junction there was marked thickening, and involvement by tumor growth was noted.

Several sections were taken through different portions of the kidney, and microscopically all showed a similar picture, although in some portions the

Fig. 1 (case 1).—Photomicrograph showing papillary carcinoma of the kidney pelvis.

structure was obscured by degenerative changes. The outstanding features were the large masses and columns of large deeply staining, chromatic stratified epithelial cells which were growing in wild profusion in every direction and infiltrating deeply (fig. 1). Practically no normal renal structure was apparent in any area. Pearl formations were seen in abundance.

The diagnosis was squamous cell carcinoma originating from the right renal pelvis.

CASE 2.—A man 52 years of age was first seen at the clinic on April 14, 1933. His chief complaint was of pain in the back, which had been present for ten weeks. The pain occurred chiefly on the right side and radiated down the right thigh and to the right groin. For two weeks a dull, aching pain had persisted. At the onset of the symptoms hematuria had occurred and had been present at intervals; occasionally clots were passed. Nocturia had been present for one year. During the preceding ten weeks, 10 pounds (4.5 Kg.) in weight had been lost.

Physical Examination.—No abnormality was discovered in the abdomen except muscular spasm over the right lumbar region and tenderness to percussion in

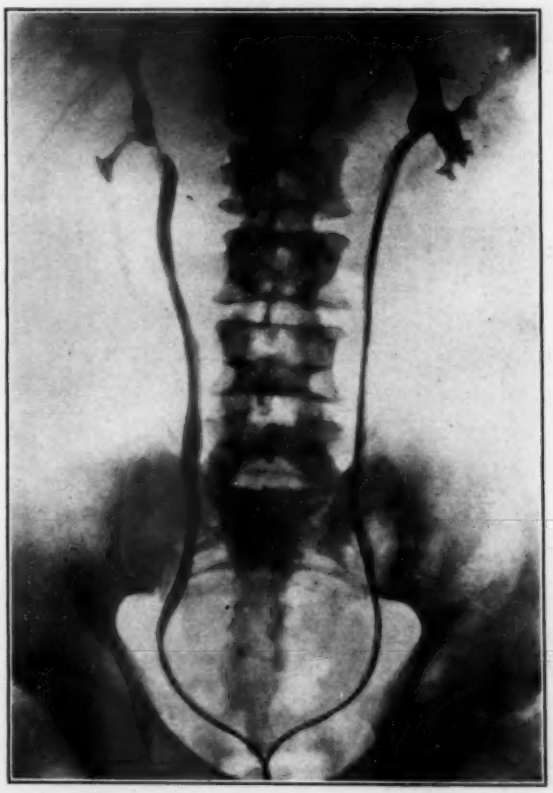

Fig. 2 (case 2).—Bilateral pyelogram showing the left kidney to be normal except for a little rotation on the long axis. The lower calix of the right kidney is normal, but there are compression and infiltration in the upper three quarters of the kidney.

the same area. Slight lordosis was present. The prostate showed enlargement of grade 2; it was firm but not hard or fixed.

Laboratory Data.—Examination of the urine showed the specific gravity to be 1.015. The urine gave an acid reaction; a trace of albumin was present, but there was no sugar. Microscopically there were numerous red blood cells and 15 to 20 white blood cells per high power field. Examination of the blood

revealed 5,490,000 red cells and 10,800 white cells per cubic millimeter; hemoglobin, 87 per cent; neutrophils, 87 per cent; lymphocytes, 8 per cent, and monocytes, 5 per cent. The value for sugar was 110 mg., and that for urea 38 mg., per hundred cubic centimeters of blood. The Wassermann test gave a negative reaction. A roentgenogram of the chest revealed no abnormalities.

Roentgen examination of the kidneys, the ureters and the bladder showed no evidence of stones or other pathologic change in the urinary tract.

Fig. 3 (case 2).—Photomicrograph showing a squamous cell carcinoma of the kidney pelvis.

Cystoscopic Examination.—The cystoscope was introduced without difficulty. The bladder contained 20 cc. of clear residual urine, and there were no stones, ulcers, tumors or diverticula. Five cubic centimeters of indigo carmine was injected intravenously, and it appeared from the left kidney in four and one-half minutes, with 4 plus concentration, and from the right in six and one-half minutes, with 2 plus concentration. Catheters were passed without obstruction to both pelves, and specimens of urine were secured.

A bilateral pyelogram was made after injection of 7 cc. of solution on the left and 6 cc. on the right. This showed the left kidney to be normal except for a little rotation on the long axis. The lower calix of the right kidney was normal, but compression and infiltration were observed in the upper three quarters of the kidney (fig. 2).

Diagnosis and Treatment.—The diagnosis was carcinoma of the right kidney.

Fig. 4 (case 2).—Photomicrograph showing a blood vessel completely filled with tumor cells.

Roentgen therapy was advised, and six doses at 200 kilovolts, with filtration equivalent to 1 millimeter of copper (1,750 roentgens anteriorly and posteriorly), were given, the kidney receiving about 1,500 roentgens.

Operation.—Nephrectomy on the right was performed on April 28.

Pathologic Examination.—Grossly the specimen consisted of the right kidney and 6 cm. of the ureter. Its weight was 208 Gm. On the anterior surface of the kidney, extending out of the hilus, there was an oval, bulging tumor mass to

which the capsule of the kidney and the perirenal fat were adherent. The tumor measured 7.5 by 6 cm. On section through the kidney a large tumor mass was seen, which had a yellowish gray, moth-eaten appearance. It was not well circumscribed but appeared diffusely infiltrative. The pelvis and calixes appeared somewhat compressed by the tumor mass.

Microscopically, sections through the pelvis of the kidney showed normal pelvic mucosa in some places but complete loss of mucosa in other areas. There were metaplastic changes in the epithelium at other sites. Ulceration of the mucosa and replacement by an infiltrating squamous cell carcinomatous growth were observed (fig. 3). The cells were of the large squamous type, with some tendency to form keratohyaline material but with no pearl formation. The tumor was diffusely infiltrating outward from the renal pelvis into the surrounding medulla, cortex and peripelvic fat. In one section a large branch of the renal artery was intensively infiltrated, and the lumen was occluded by tumor cells (fig. 4). A branch of the renal vein was involved in a similar manner. Throughout the area occupied by the tumor there were atrophy and fibrosis of the kidney tissue.

The pathologic diagnosis was squamous cell carcinoma originating in the pelvis of the right kidney.

Course.—The patient's convalescence was uninterrupted, and he was discharged from the hospital eighteen days after the operation. Roentgen therapy was again instituted.

The patient returned on July 17, two months after discharge from the hospital, complaining of pain in the left side of the chest. Roentgen examination was made, and the following report was given: "The chest shows metastatic malignant changes. There is one rather large nodule in the upper portion of the left lung, as well as nodules in the upper lobe of the right lung."

The patient died from metastases on September 7.

CASE 3.—A man 51 years of age was admitted to the clinic on Dec. 30, 1933, because of pain in the region of the right kidney. He stated that during the preceding three years a dull, aching pain had frequently been present in the right side and was referred to the back and to the right upper quadrant of the abdomen. The periods of discomfort persisted for two or three days and were followed by several weeks of freedom from pain. Blood had been present in the urine at intervals during the last three years. Nocturia (two to three times) had also been noted. One year before this examination the patient had fallen, and at that time a diagnosis of "misplaced kidney" was made.

Physical Examination.—Palpation revealed a large right kidney which was somewhat tender and only partially movable.

Laboratory Data.—The specific gravity of the urine was 1.015; the reaction was acid, and albumin (2 plus) was present. There was no sugar. Microscopically, numerous red blood cells were found, and there were 15 to 20 white blood cells per high power field. The value for urea was 39 mg., and that for sugar 118 mg., per hundred cubic centimeters of blood. A blood count showed 5,290,000 red cells and 10,450 white cells per cubic millimeter; hemoglobin 84 per cent; neutrophils, 84 per cent; eosinophils, 1 per cent; lymphocytes, 12 per cent, and monocytes, 3 per cent. The Wassermann reaction of the blood was negative.

Roentgen examination of the kidneys, the ureters and the bladder revealed huge calcific deposits in the right kidney (fig. 5). This kidney was very large, and a final diagnosis of calculous pyonephrosis was made.

Nephrectomy was performed Jan. 9, 1934, and an enormous kidney containing large and small calculi was removed (fig. 6).

Pathologic Examination.—The specimen was the right kidney. It was received in the laboratory already sectioned. It measured 19.5 by 11 by 5.5 cm. It contained numerous stones and one very large calculus. The capsule was thickened and was adherent to the kidney. On section no normal-appearing cortex or medullary tissue was present. The pelvis and calices were dilated and thickened. At the lower pole, which was the site occupied by the large stone, leukoplakia was present. This was a pearly gray, membrane-like structure which was very

Fig. 5 (case 3).—Roentgenogram showing huge calcific deposits in the right kidney.

adherent. It measured 16 by 9 cm. In a few areas, papillomatous projections of the same structure appeared. There was considerable fibrous thickening in the wall of the pelvis near the ureteropelvic junction and in the septums between the calices.

Microscopically (figs. 7 and 8), sections through the kidney showed atrophy, degeneration, fibrosis and chronic inflammatory changes in the cortex and medulla. There were also ulceration of the pelvic mucosa and diffuse chronic inflammatory infiltration. In several of the sections, small areas and solid nests of rather large epithelial cells were present in the subepithelial layers of the mucosa.

Fig. 6 (case 3).—Kidney after removal, showing large and small calculi.

Fig. 7 (case 3).—Photomicrograph showing leukemia and squamous cell carcinoma.

Several sections from the dilated pelvis showed ulceration and chronic inflammation, and in other areas there was complete replacement of the normal epithelium by keratinizing stratified squamous epithelium. There was extensive infiltration of the subepithelial layers of the pelvis by small and large solid masses of stratified squamous epithelium. In some areas the entire pelvic wall was infiltreated, and tumor masses were infiltrating the peripelvic fat.

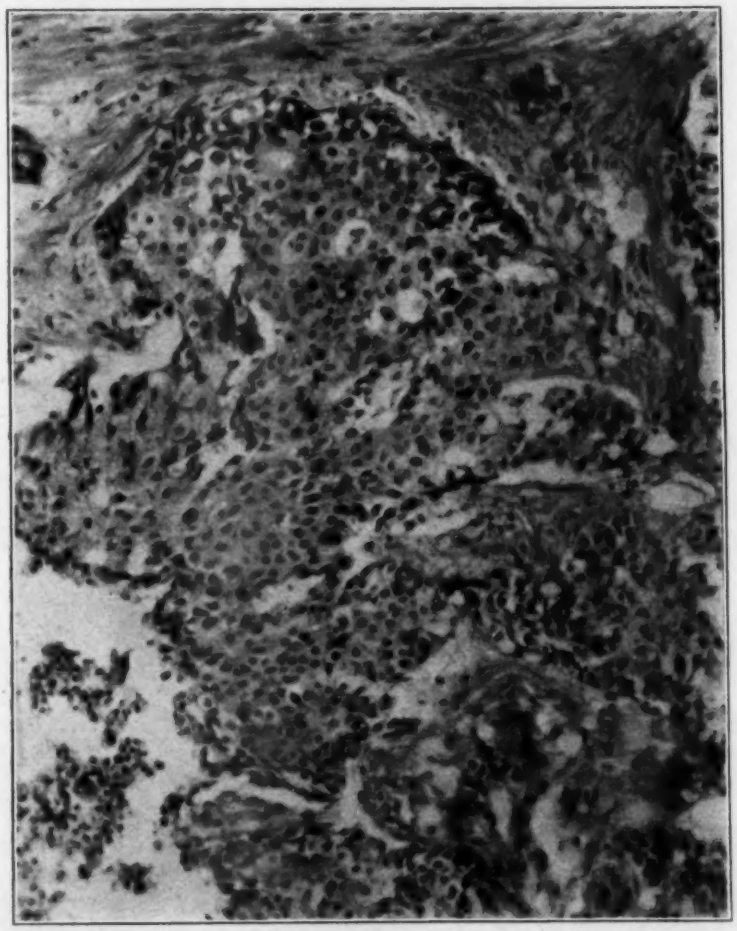

Fig. 8 (case 3).—Photomicrograph showing a squamous cell carcinoma.

The diagnosis was: nephrolithiasis of the right kidney, leukoplakia, squamous cell carcinoma of the right kidney, pyonephrosis and chronic pyelitis.

Course.—The patient died in the hospital from bronchopneumonia on the twenty-seventh day after the operation.

Postmortem examination revealed bronchopneumonia and also metastases in the perirenal fat, the periaortic nodes and the lungs.

Case 4.—A woman 49 years of age was first seen by me on June 15, 1932. Her chief complaint was of pain in the left side. Two years before this examina-

Fig. 9 (case 4).—Pyelogram showing a filling defect in the lower calix of the left kidney.

Fig. 10 (case 4).—Pyelogram made eleven months after figure 9, showing a filling defect in the pelvis of the left kidney and narrowing of the ureteropelvic junction.

tion she had had a severe attack of pain in the same side, which lasted for a few hours. Two weeks later a similar attack occurred, after which she was free from symptoms until five months before the present examination. The pains began in the left side of the back and radiated around to the groin and to the upper part of the thigh. They were so severe that morphine was required to relieve them. For five months some pain had been present constantly. After the

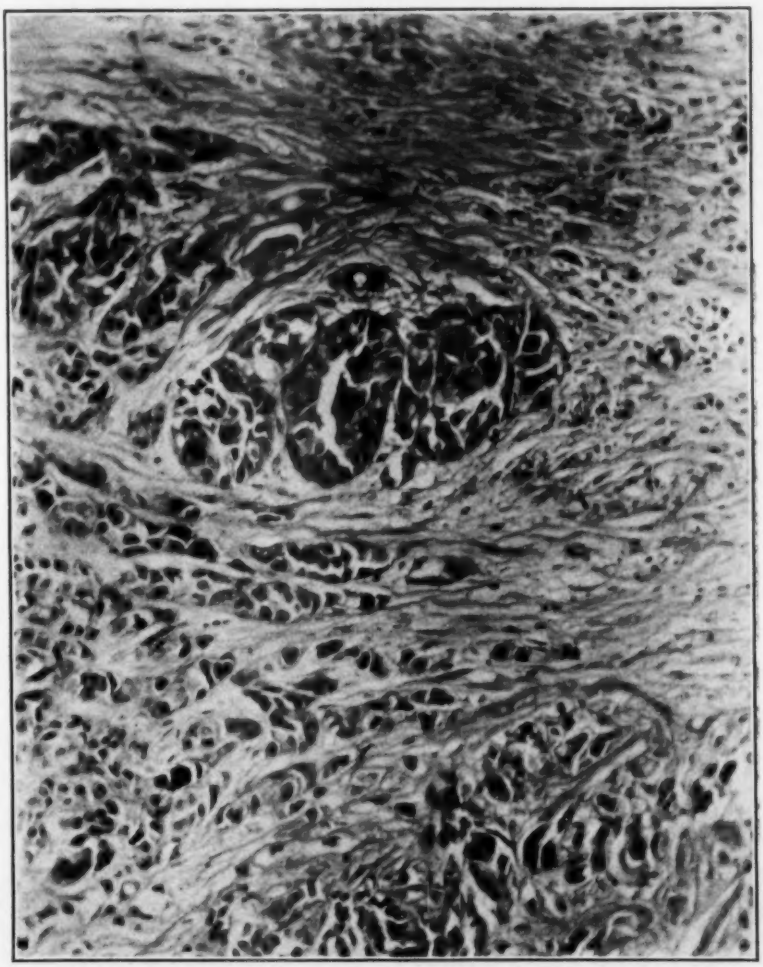

Fig. 11 (case 4).—Photomicrograph showing a papillary carcinoma of the kidney pelvis.

last attack a large amount of blood had been passed, and since that time hematuria had been present for two or three days of each week.

Physical Examination.—No abnormality was revealed, and neither kidney was palpable.

A roentgenogram of the kidneys, the ureters and the bladder showed no abnormality.

Laboratory Data.—The specific gravity of the urine was 1.024; the urine was alkaline. There was a trace of albumin. No sugar was present. Microscopically, 50 to 100 red blood cells and 2 or 3 white blood cells per high power field were found. Examination of the blood showed 5,140,000 red cells and 9,250 white cells per cubic millimeter; hemoglobin 80 per cent; neutrophils, 67 per cent; eosinophils, 1 per cent; lymphocytes, 28 per cent, and monocytes, 4 per cent. The value for sugar was 91 mg., and that for urea 33 mg., per hundred cubic centimeters of blood. The Wassermann reaction of the blood was negative.

Cystoscopic Examination.—The cystoscope was introduced with ease. The capacity of the bladder was 200 cc. The bladder showed no stone, ulcer, tumor or diverticulum. Five cubic centimeters of indigo carmine was injected intravenously and was seen spurting from the ureteral orifices in four and one-half minutes, with a 4 plus concentration. A catheter was passed unobstructed to the left kidney pelvis, and after injection of 8 cc. of solution a pyelogram was taken.

Pyelogram.—The pyelogram showed a filling defect in the lower calix of the left kidney. It was felt that this might be due to incomplete filling, to a blood clot or to tuberculosis (fig. 9).

The patient was advised to await any further development of symptoms. She returned in July 1933, eleven months after the initial examination, and reported that hematuria had been present at intervals. A pyelogram taken at this time showed a filling defect in the pelvis of the left kidney and narrowing of the ureteropelvic junction, which suggested the presence of a neoplasm (fig. 10). Nephrectomy was advised, and the left kidney was removed June 8, 1935.

Pathologic Examination.—The specimen consisted of the left kidney with 7 cm. of the ureter. It measured 11 cm. longitudinally, 6 cm. transversely and 4.5 cm. anteroposteriorly. The weight of the specimen was 140 Gm. The capsule stripped readily, exposing a smooth, light brown cortical surface in which fetal lobulations were fairly well marked. The lower pole for a distance of 4 cm. was shrunken, atrophic and pale in contrast to the remainder of the kidney. On section this lower portion of the kidney was seen to be largely filled and infiltrated with a hard opaque yellowish white growth measuring 2 cm. on the cut surface. A tumor arose from the pelvis in the region of the lower calix, which it partially filled. The tumor measured 2 by 1 by 1 cm. It was flat and had a broad base. The pelvic mucosa appeared thickened and edematous.

Microscopically (fig. 11), section of the tumor near the ureteropelvic junction showed a somewhat papillary growth of pelvic epithelium, with invasion of the underlying submucosal and peripelvic tissue by large and small solid masses of squamous epithelium showing some keratinization. The tumor cells varied greatly; mitotic figures were scarce. The growth was diffusely infiltrating the medulla of the kidney and extending toward the cortex.

The diagnosis was squamous cell carcinoma of the left kidney pelvis.

Progress.—Convalescence was uneventful. Postoperatively, high voltage roentgen therapy was administered. The patient was last seen June 1, 1936. Her condition was excellent, and there was no evidence of metastasis. This patient is living and well three years after removal of the kidney.

CASE 5.—A man 58 years of age entered the clinic on Nov. 1, 1932, because of pain in the back and blood in the urine. He had been perfectly well until three months prior to his admission to the hospital, when he had had a painless attack of hematuria. Since that time there had been intervals during which the

presence of blood in the urine was not noticed. During the preceding two months he had been aware of a dull, aching pain in the right side of the back and in the thigh. He had lost 30 pounds (13.6 Kg.) in weight in the previous six months.

Physical Examination.—There was a palpable mass in the right upper part of the abdomen; this was firm but movable. Little tenderness was elicited on palpation.

Laboratory Data.—The specific gravity of the urine was 1.007; the urine was alkaline; there was a trace of albumin but no sugar. Microscopically, red blood cells (3 plus) and white blood cells (1 plus) were observed. Examination of the blood showed 4,740,000 red cells and 7,850 white cells per cubic millimeter, with 80 per cent of hemoglobin. A differential count revealed no abnormality. The value for sugar was 102 mg., and that for urea 27 mg., per hundred cubic centimeters of blood. The Wassermann reaction of the blood was negative.

Roentgen examination showed a large mass in the region of the right kidney. The chest was normal, and there was no roentgen evidence of pathologic change in the bony pelves.

Cystoscopic Examination.—The cystoscope was introduced fairly easily. The bladder contained 40 cc. of residual urine. Both ureteral orifices were seen, and the catheters were passed without obstruction to both kidney pelves. No secretion was demonstrable from the right kidney. After the injection of 7 cc. of solution on the left side and 5 cc. on the right side a bilateral pyelogram was taken.

The pyelogram revealed a tumor of the right kidney.

An intravenous urogram did not give findings satisfactory for diagnosis.

The final diagnosis was tumor of the right kidney.

A nephrectomy on the right side was performed with some difficulty on November 12. A plug of tumor was present in the renal vein; however, a pedicle clamp could be placed below the involved portion of the vein. This tore an opening in the vena cava, which was sutured, and a blood transfusion was administered at the completion of the operation.

Pathologic Examination.—The kidney measured 9.5 by 6 by 5 cm. It was firm, and the capsule stripped with some difficulty, exposing a smooth yellowish brown cortex. Section through the kidney showed a moderately dilated pelvis, the mucosa of which was rather rough and had a moth-eaten appearance and from which there were numerous small papillary projections. The peripelvic fat was hard and fibrous and was apparently infiltrated with tumor tissue. At the hilus of the kidney the peripelvic fat, the ureter and the blood vessels were all involved, and a small probe was passed through the ureteropelvic junction with difficulty.

Microscopically, sections through the kidney, including the pelvis, showed a thickened pelvic surface covered by single and multiple layers of rather large, atypical epithelial cells having an epidermoid appearance but showing no keratinization. Extending upward and outward from the pelvis were small and large solid masses of similar epithelial cells diffusely infiltrating the medullar cortex and the capsule proper of the kidney. Section of the fatty extrarenal tissue showed diffuse infiltration by small masses of large epithelial cells similar to those which have been mentioned.

The diagnosis was squamous cell carcinoma of the renal pelvis.

Course.—Convalescence from the operative procedure was uneventful, but a metastatic lesion of the upper end of the left femur was found on December 16, and the patient died three years later.

ETIOLOGY

The relation between leukoplakia and squamous cell carcinoma of the renal pelvis is frequently cited in the literature. In 1929, Kutzmann [6] reviewed 67 cases of leukoplakia of the renal pelvis and concluded that this condition might be a forerunner of squamous cell carcinoma. A coincidental involvement of the renal pelvis occurred in 11.9 per cent of his cases. Patch [7] collected 12 cases from the literature and added 1 of his own, in which he demonstrated the transitional stages between leukoplakia and squamous cell carcinoma. He felt that such a condition is definitely precancerous and that his findings offered evidence in favor of a transitional stage between leukoplakia and squamous cell carcinoma. Cabot's [8] findings seem to confirm the relation between these two pathologic entities. For his patient a suprapubic cystotomy was performed, and a thick sheet of pearly tissue was removed from the vesical wall. A diagnosis of leukoplakia or pachyderma vesicae was made. Pavement epithelial cells were found in the bladder washings. Eight years later the patient returned, and a fistula was found above the pubis. The bladder was explored, and a portion which was removed showed squamous cell carcinoma.

In the case reported by Hinman and his associates,[9] sections of the renal pelvis showed definite leukoplakia; however, in some sections atypical epithelial cells were present, and the leukoplakic areas in certain sites showed a papillary downgrowth with a beginning break in the basement membrane. He stated that the microscopic picture closely resembled that of carcinoma and that such a condition should be considered precancerous.

The striking relation between renal calculi and squamous cell carcinoma has been noted by many observers. It is believed by some authors that the development of metaplastic changes may be induced by long-continued irritation from chronic inflammation or from renal calculi. This seems especially probable since a review of a number of case reports shows that the presence of calculi or of chronic inflammation of the renal pelvis seems definitely to antedate the malignant lesion.

Hallé [10] stated that chronic inflammation or the presence of calculi may initiate an epithelial change in the mucosa of the urinary tract

6. Kutzmann, A. A.: Leukoplakia of the Renal Pelvis, Arch. Surg. **19**:871-897 (Nov.) 1929.

7. Patch, F. S.: The Association Between Leukoplakia and Squamous Cell Carcinoma in the Upper Urinary Tract, New England J. Med. **200**:423-437 (Feb. 28) 1929.

8. Cabot, cited by Patch.[7]

9. Hinman, F.; Gibson, T. E., and Kutzmann, A.: Leukoplakia of the Kidney Pelvis, Surg., Gynec. & Obst. **39**:472-489 (Oct.) 1924.

10. Hallé, cited by Kretschmer.[2]

and that the normal epithelium becomes transformed into stratified squamous epithelium with epidermoid characteristics. Thus the presence of a squamous cell carcinoma of the renal pelvis, which under normal conditions does not contain squamous epithelium, may be explained by metaplasia of the normal epithelium to stratified squamous epithelium and the formation of leukoplakia, which in some instances may undergo a carcinomatous change in certain areas. Albarran [11] expressed the opinion that chronic irritation by calculi may be conducive to the formation of leukoplakia and that the latter may be the first stage in the development of squamous cell carcinoma. The relation between leukoplakia and the subsequent development of carcinoma in other parts of the body is frequently mentioned.

It is also of interest to note that epithelial changes may occur in the presence of vitamin A deficiency, as reported by Wolbach [12] and as I noted during my experimental work on the formation of urinary calculi in white rats.[13] Wolbach stated:

> In vitamin A deficiency, in the human called xerophthalmia or keratomalacia, we found in rats and guinea pigs a very striking and extensively distributed metaplasia of epithelium in the conjunctivae, the ocular glands, alimentary tract, respiratory tract, and genito-urinary tract. In these locations, the epithelium becomes replaced by a stratified, keratinizing epithelium, a condition similar to or comparable with leukoplakia.

In analyzing clinical cases, however, one finds that renal calculi, long-continued chronic inflammation and leukoplakia are the predominating precursors of squamous cell carcinoma of the renal pelvis.

FREQUENCY

Fifty-nine cases of squamous cell carcinoma of the pelvis of the kidney have previously been reported in the literature. McKenzie and Ratner [14] have stated that tumors of the renal pelvis comprise from 5 to 7 per cent of all renal tumors. Kretschmer,[2] in reviewing 43 cases of nonpapillary tumors of the renal pelvis, noted the presence of epidermoid structure in 17 instances. In a series of 35 renal tumors reported by Bowen and Bennett,[15] 5 squamous cell carcinomas were

11. Albarran, J.: Neoplasmes primitifs du bassinet et de l'urétère, Ann. d. mal. d. org. génito-urin. **18**:701, 1918 and 1179, 1900.

12. Wolbach, S. B., in discussion on Patch.[7]

13. Higgins, C. C.: Experimental Production of Urinary Calculi, J. Urol. **29**: 157-170 (Feb.) 1933.

14. McKenzie, D. W., and Ratner, M.: Tumors of the Renal Pelvis: Review of the Literature and Report of a Case, J. Urol. **28**:405-418 (Oct.) 1932.

15. Bowen, J. A., and Bennett, G. A.: Squamous Cell Carcinoma of the Kidney Pelvis, J. Urol. **24**:495-501 (Nov.) 1930.

found microscopically. Patch [7] collected a series of 152 cases of squamous cell carcinoma of the kidneys, the ureters and the bladder. Jocelyn Swan [16] in 1933, in a personal series of 65 cases of renal tumor, noted 2 lesions which were classified as squamous epithelioma.

Since the review of the literature by Gilbert and MacMillan [3] in 1934, a case has been reported by Silverstone [4] in 1935, and in 1936 Nicholson [5] reported the occurrence of a squamous cell carcinoma involving a horseshoe kidney. This, with my series of five squamous cell tumors, makes a total of 64 cases.

AGE

In the majority of reported cases the lesions have occurred in patients in the fifth decade of life, the average age being 56 years. In the Cleveland Clinic series the ages were 41, 52, 51, 49 and 58 years, respectively. Silverstone [4] stated that 50 per cent of the lesions occur in patients between the ages of 40 and 60. One patient cited by Kischensky [17] was 32 years of age, while Simpson [18] reported the case of a patient who was 79.

SEX

In the cases reported the tumors have occurred in 36 male and 28 female patients. Gilbert and MacMillan, in reviewing 57 cases, found that the tumor occurred in 31 males and 26 females. This is in contrast to some reports in the literature, in which it is stated that the tumor occurs twice as frequently in the male sex. In this series there were 3 female and 2 male patients.

KIDNEY INVOLVED

Gilbert and MacMillan [3] stated that from the data available in their cases 26 lesions involved the right and 26 the left kidney. The right kidney contained the tumor in the case reported by Silverstone,[4] while the tumor reported by Nicholson [5] occurred in a horseshoe kidney. In this series, the right kidney contained the tumor in 4 instances and the left kidney in 1.

SYMPTOMS

No definite symptoms are pathognomonic of squamous cell carcinoma of the renal pelvis. In many cases reported in the literature the symptoms have been referable to a coexisting renal calculus. Some observers

16. Swan, R. H. J.: New Growths of Kidney, with an Analysis of Sixty-Five Cases, Brit. M. J. **1**:606-610 (April 8) 1933.

17. Kischensky, D. P., cited by Gilbert.[3]

18. Simpson, C. M.: Malignant Tumors of the Renal Pelvis, Texas State J. Med. **26**:787-791 (March) 1931.

have stated that hematuria rarely occurs in association with this type of tumor, owing to its relative avascularity in comparison with papillary tumors; however, this symptom was present in each of my 5 patients. Kretschmer [2] stated that hematuria is one of the most important symptoms of tumor of the renal pelvis and that it may be the only symptom. Usually the bleeding is not accompanied by pain.

Each of my patients complained of symptoms referable to pyuria, which was due either to a calculus or to chronic inflammation, and of pain in the back. The latter symptom has been present in 43 per cent of cases in the collected series.

Loss of weight is a late manifestation, usually occurring after metastases have developed. Scholl [19] has stated that the condition may produce no symptoms and that when obstruction at the ureteropelvic junction occurs it is from slow occlusion, which at times causes enormous dilatation of the renal pelvis but little pain.

DIAGNOSIS

Early diagnosis is essential; however, this may be difficult even when all available facilities are employed. Squamous cell carcinoma must be differentiated from tumor involving the renal parenchyma, from nonopaque calculi in the renal pelvis and from renal tuberculosis in an early stage.

The presence of a palpable mass may direct attention to the possibility of a renal tumor, such as occurred in 1 of my patients. Owing to the development of hydronephrosis, as Scholl has stated, the mass may attain considerable size. The initial roentgenogram may reveal enlargement of the kidney, thus indicating the need for cystoscopic investigation and pyelography.

Pyelography is the most important means of establishing a diagnosis. A persistent filling defect in the renal calix must be differentiated from early renal tuberculosis, as was considered in 1 of my cases. Here a clinical history of irritability of the bladder and the cystoscopic findings are of value in ruling out renal tuberculosis. Examination of the urine for tubercle bacilli and also inoculation of guinea pigs may be of value. Occasionally the presence of a calculus may mask the true condition, and the malignant tumor may be found only after examination of the specimen which has been removed. A pneumopyelogram or variation in the concentration of the pyelographic medium may be of value in determining the presence of a nonopaque calculus. In the majority of cases, a tumor primary in the renal parenchyma will present pyelographic evidence that the lesion is not primary in the renal pelvis.

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19. Scholl, A. J.: Squamous Cell Tumors of the Kidney Associated with Stone. J. A. M. A. **100**:236-238 (Jan. 28) 1933.

Tests of renal function obviously are of value in ascertaining the function not only of the kidney containing the tumor but also of the opposite kidney.

COEXISTING PATHOLOGIC CONDITIONS

Leukoplakia and renal calculi are the two conditions most frequently associated with squamous cell carcinoma of the renal pelvis. A chronic inflammatory process often is present. Darmady,[20] Wells,[21] Scholl,[19] Menetrier and Martinez,[22] Kretschmer,[23] Patch,[7] Hinman[9] and others have discussed such coexisting pathologic conditions. Bugbee[24] cited a case in which the tumor was associated with an impacted ureteral calculus. It is stated that renal calculi are found in the presence of squamous cell carcinoma of the kidney pelvis in approximately 52 per cent of cases. Hydronephrosis and pyonephrosis have been present in many instances. This was due to obstruction at the ureteropelvic junction, which was produced by involvement by the malignant growth or by a calculus in the renal pelvis. Squamous cell carcinoma has been reported as occurring in horseshoe kidneys in 4 instances, by Primrose,[25] Willan,[26] Melen and Gasper,[27] and Nicholson.[5]

PATHOLOGIC PICTURE

Two types of lesion predominate. In the first type the tumor cells invade the renal parenchyma early and eventually replace it. Silverstone[4] stated that as the growth progresses to the periphery the epithelium becomes more anaplastic, more rapidly growing and more primitive, so that it resembles carcinoma simplex. He stated that this type is most frequently associated with calculi. Such findings were not noticed in the pathologic specimens in this series.

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20. Darmady, E. M., cited by Scholl.[19]

21. Wells, H. G.: Carcinoma of the Kidney as a Sequel of Calculi, Arch. Surg. **5**:356-365 (Sept.) 1922.

22. Menetrier, M. P., and Martinez, M.: Lithiase et cancer du rein, Bull. Acad. de méd., Paris **79**:65-74 (Jan. 22) 1918.

23. Kretschmer, H. L.: Leukoplakia of the Kidney Pelvis, Arch. Surg. **5**:348-355 (Sept.) 1922.

24. Bugbee, H.: Primary Carcinoma of Kidney with Impacted Ureteral Calculus, J. Urol. **5**:267-278 (April) 1921.

25. Primrose, A.: Squamous Cell Carcinoma of the Kidney: Report of a Case Occurring in a Horseshoe Kidney Complicated by Calculus Pyonephrosis, J. A. M. A. **75**:12-16 (July 3) 1920.

26. Willan, R. J.: Giant Renal Calculus with Epithelioma in a Horseshoe Kidney, Brit. J. Surg. **16**:317-321 (Oct.) 1928.

27. Melen, D. R., and Gasper, I.: Calculus Pyonephrosis in Carcinomatous Horseshoe Kidney, J. Urol. **25**:43-52 (Jan.) 1931.

The second type of lesion is confined chiefly to the renal pelvis. This is covered by a tumor mass which in some areas has a papillary appearance. With this type, involvement of the ureteropelvic junction occurs earlier, and extensive hydronephrosis with atrophy of the renal parenchyma is found.

Metastases.—Metastases are stated to occur early and are widespread, dissemination through the blood stream being evidenced by lesions in the lungs, the liver and the bones. Metastases also invade local lymphatic glands. However, in many instances a diagnosis is not established early and the carcinoma has extended beyond the confines of the kidney when first recognized. As in many instances calculi and leukoplakia coexist with or precede the malignant process, the carcinoma is undoubtedly present for a long period but is not suspected.

In 19 autopsy studies cited by Kretschmer,[2] the liver was found to be involved in 8 instances, the peritoneum in 3, the lungs and pleura in 5, the bones in 5 and other organs in isolated cases. In this series, metastasis to the lungs occurred in 1 case. In the second case the perirenal fat, the periaortic lymph nodes and the lungs were involved. In the third case an autopsy of the entire body was not done; in the fourth case there was no evidence of metastasis, and in the fifth case metastasis to the upper end of the femur occurred.

TREATMENT

Early diagnosis followed by nephrectomy is the procedure of choice. In this series, in which preoperative high voltage roentgen therapy was employed, there was no evidence of a reduction in the size of the tumor. Postoperative roentgen therapy is advisable. Diagnosis is frequently not established until late in the course of the disease, and metastases may be present when the patient first consults the physician.

PROGNOSIS AND END RESULTS

The prognosis is grave, owing to the frequency of metastasis. In a review of the literature I was unable to find the report of a patient who was free from metastases at the end of five years. In 5 of the cases reviewed by Scholl,[19] 4 patients died during the first four months after operation, and 1 was living six months after operation. Kretschmer [2] reported that the immediate mortality was high for nonpapillary tumors of the renal pelvis. Of 30 patients on whom operation was performed, 16 died immediately or soon after operation, the operative mortality of the series being 53.3 per cent.

The average duration of life was seven months and fifteen days. In this series 1 patient died from bronchopneumonia twenty-eight days

after operation. The second died five months after operation with metastases in the lungs; the third died from generalized metastases one month after operation. The fourth patient is living and well three years and eight months after operation, with no evidence of metastasis, and the fifth patient died of metastases two years and nine months after operation.

CONCLUSIONS

1. Squamous cell carcinoma of the renal pelvis is relatively rare.

2. Diagnosis is not established early, and metastases are frequently present when the patient is first seen by the physician.

3. The prognosis is grave.

4. The importance of complete urologic investigation in cases of hematuria is well demonstrated by a study of this series of tumors.

GROWTH IN LENGTH OF THE VERTEBRAE

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Growth in length of the long bones in man and animals is caused by a purposeful multiplication of cartilage cells of the epiphysial cartilage plates. It is held that in the vertebrae of man the center grows within itself until it occupies the entire cartilaginous area free to it and there is not the characteristic columnar formation of cartilage cells. The epiphysis is therefore not a growth body but an organ of fixation concerned with the architecture of the spine. It is even claimed that in animals, in spite of the fact that the epiphysis is a complete disk, it does not share in the process of longitudinal growth.

The importance of this problem warranted further study of the growth of the vertebrae of animals. On gross examination of a vertebra of a dog a cartilage plate is found at each end. The microscopic appearance of this plate is similar in structure to the epiphysial plate of any long bone (fig. 1).

In order to determine whether growth takes place at the epiphysial cartilage plate a series of experiments were performed, in which markers were placed in the bodies and in the epiphyses of the vertebrae. If the markers in the epiphysis and those in the body of a vertebra separated, it would show that the epiphysial plate was functioning to increase length. If the markers in the body did not separate, it would indicate that there was no interstitial growth.

The following experiments were performed on dogs under ether anesthesia.

Dog 1 (aged 2 months).—On Nov. 5, 1937, through an abdominal incision, the bodies of the second and third lumbar vertebrae were exposed. After identification of the epiphysial plate a silver wire marker was inserted into the body of the second lumbar vertebra. Into the third lumbar vertebra four markers were placed in different parts. One was placed in the lower epiphysis and three in the body (fig. 2).

A roentgenogram (fig. 3) taken one hundred and twelve days later (February 25) showed the markers in the body of the fourth lumbar vertebra to be the same distance apart and in the same relative position as at the time of insertion. The marker in the lower epiphysis of the fourth lumbar vertebra had separated from these three, owing to growth at the intervening epiphysial cartilage plate. The marker in the body of the third lumbar vertebra had separated a greater distance because of the growth of the lower epiphysial plate of the second and the upper plate of the third lumbar vertebrae.

From the Surgical Laboratory, Stanford Medical School.

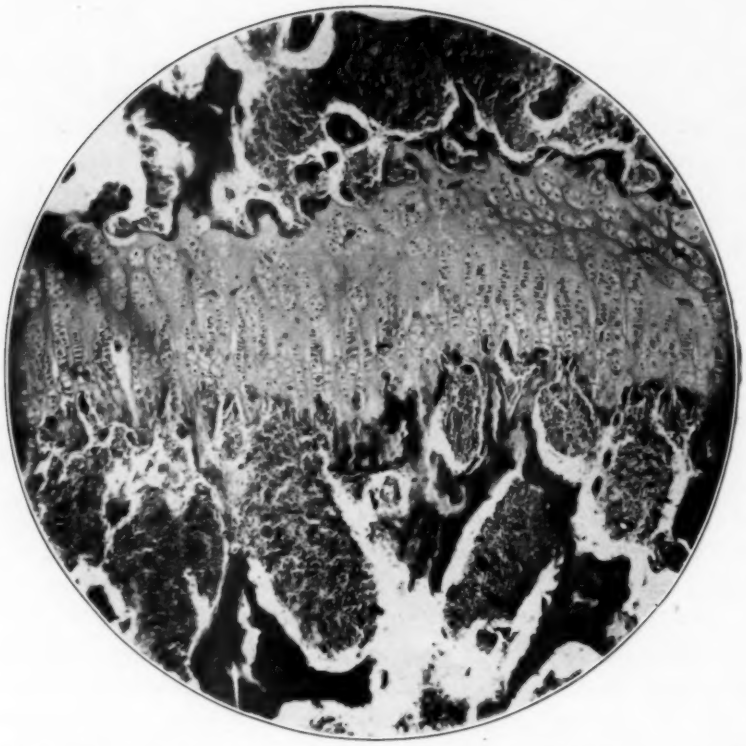

Fig. 1.—Photomicrograph of the epiphysial cartilage plate from a vertebra of a dog 2 months old.

Fig. 2 (dog 1).—Position of the markers in the vertebrae at the beginning of the experiment. The lowest marker is not in the vertebrae.

Fig. 3 (dog 1).—Position of the markers one hundred and twelve days after insertion. Note that the markers in the vertebral bodies have not separated from each other, while those in the epiphyses have separated from those in the bodies. Compare with figure 2.

Fig. 4 (dog 2).—Position of the markers in the vertebral bodies at the beginning of the experiment.

Dog 2 (aged 2 months).—On Nov. 5, 1937, through an abdominal incision, the fourth and fifth lumbar vertebrae were exposed. Three markers were placed in the fourth, two in the body and one in the lower epiphysis. In the fourth lumbar vertebra a marker was placed in each epiphysis and two in the body (fig. 4).

The roentgenogram (fig. 5), taken one hundred and twelve days later (February 25) showed no change in the position of the markers in the body of the fourth lumbar vertebra but a separation of the markers in the epiphysis caused by growth of the intervening epiphysial cartilage plate. In the fifth lumbar vertebra the

Fig. 5 (dog 2).—Roentgenogram taken one hundred and twelve days after insertion of the markers. The markers in the vertebral bodies occupy the same position. The markers in the epiphyses have separated from those of the bodies, owing to growth at the epiphysial plates. Compare with figure 4.

two markers in the body were in the same position, but the markers in the upper and lower epiphyses had separated from those in the body, owing to the growth at the intervening epiphysial plates.

COMMENT

The results of these experiments on dogs show that growth in length of the vertebrae occurs in a manner similar to that of growth in length of the long bones, namely, by proliferation at the epiphysial cartilage plate.

There is no interstitial growth in the body of the vertebrae, as the markers placed in the bodies remained in the same relative positions as at the time of insertion. In the vertebrae of the dog the epiphysial cartilage plate is the growth body, but it is held that in man there is no such structure. Further study may give some clue as to the exact mechanism in man and may help to explain this single point of difference in osseous growth in man and in experimental animals. It is possible that some other interpretation of the findings in man may allow a correlation of the process with that of the lower animals.

CONCLUSIONS

1. The vertebrae of the dog increase in length as do the long bones, i. e., by a purposeful multiplication of the column of cells at the epiphysial cartilage plate.

2. There is no interstitial growth in the bodies of the vertebrae.

450 Sutter Street.

POSTERIOR DISLOCATION OF LOWER FEMORAL EPIPHYSIS IN BREECH DELIVERY

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Hartshorn [1] said that traumatic periostitis might follow breech delivery. Snedecor, Knapp and Wilson [2] reported an occurrence of traumatic ossifying periostitis after such a delivery. They reported 4 cases, the major symptoms in which were pain, swelling, limitation of motion and discoloration of the affected part. The humerus and the femur were the bones involved. Diagnosis was made late, by means of the roentgenogram. The babies were all first-born children, and it is to be assumed that the deliveries were more difficult than is usual in the case of a multipara delivered by similar presentation. Recovery was spontaneous within four to twelve weeks, and no special treatment beyond heat and the prevention of contracture was required. The injury was due, in their opinion, to (1) too strong traction on the extremity; (2) a twisting pull on the limb; (3) inequality of distribution of traction in bringing down both feet, or (4) too hasty attempt at delivery. The pathologic condition, as interpreted from the roentgenogram, was a tearing or stripping of the periosteum of either the femur or the humerus at its weakest point of attachment, the epiphysial line, with maximal stress on the proximal epiphysis. With increasing trauma, a greater part of the periosteum of the shaft was stripped. The roentgenograms at first showed normal conditions but later indicated the extent of subperiosteal stripping, after calcium salts were deposited in the subperiosteal hemorrhage. Their second case is pertinent to this subject. A subperiosteal hemorrhage elevated the periosteum of the femur, and ossification occurred beneath this stripped periosteum. The area of periosteal stripping covered most of the femoral shaft. It was widest near the line of the distal femoral epiphysis and tapered gradually proximally. The distal epiphysis was not displaced. The line of the old shaft was visible when the child was 26 days of age, surrounded by the triangular area of subperiosteal ossification. A new

From the Hospital for Joint Diseases, the Service of Dr. Leo Mayer.

1. Hartshorn, W. M.: Trauma in the New-Born, New York State J. Med. **37**:869, 1937.

2. Snedecor, S. T.; Knapp, R. E., and Wilson, H. B.: Traumatic Ossifying Periostitis of the New-Born, Surg., Gynec. & Obst. **61**:385, 1935.

shaft had been reconstructed at the age of 4 months, the cortical lines of the old shaft gradually melting away. The new shaft was a part of the old shaft and a part of the newly formed subperiosteal bone. The unneeded bone had been resorbed.

A greater injury can dislocate the lower femoral epiphysis. This is a very rare injury, and only 3 cases have been reported.

Poland [3] in his work on traumatic epiphysial separations made note of such an injury. He noted the dislocation in a fetus. He cited Mme. La Chapelle's case in which excessive traction on the foot during delivery caused a separation of the lower femoral epiphysis and the upper tibial epiphysis. The child was born dead. A specimen in the museum of the Westminster Hospital shows the left femur of a full term fetus. The distal femoral epiphysis had been violently separated and the periosteum of the shaft stripped. The middle of the shaft of the femur was incompletely fractured transversely. No history of the specimen is available.

REPORT OF CASES

CASE 1. (Truesdell [4]).—The infant was delivered by version and breech extraction because of central placenta praevia. It was difficult to deliver the after-coming head, and the body was manipulated vigorously for a long time. The right thigh was swollen and tender two days later. A roentgenogram showed an outward and backward dislocation of the lower femoral epiphysis, as indicated by the position of its center of ossification. This roentgenogram was not taken for ten days, since it was believed that the baby had an infection of the thigh. No operation was done, because the mother could not nurse the baby. A dressing was applied. Just what type of dressing was put on was not indicated, nor was the position of reduction of the limb. A roentgenogram taken when the child was 2 weeks old showed that the knee was maintained in flexion.

New bone formation about the femoral shaft was evident at the age of 2 weeks. This subperiosteal ossification extended the length of the femoral shaft and was widest at the level of the distal femoral epiphysis. The child was observed for seven months, at the end of which time it died of bronchopneumonia.

Periodic roentgenograms showed reconstruction of the femoral shaft. At the age of 2 months the femoral shaft was spadelike, thickened by the new periosteal bone. This new bone extended for a distance of three quarters of the shaft. The femur was shaping itself so that it was meeting the displaced epiphysis. At the age of 6 months the femur was still different from the normal. It looked shorter and had an anterior curvature. A new medullary cavity was forming. The epiphysis was centrally placed beneath two well formed condyles. This had been accomplished by absorption of the unneeded part of the femoral shaft. The new shaft was a combination of new periosteal bone and original shaft.

Truesdell believed that nature, unassisted, can cope successfully with this disability.

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3. Poland, J.: Traumatic Separation of the Epiphyses, London, Smith, Elder & Co., 1898, pp. 678, 683, 684 and 692.

4. Truesdell, E. D.: Birth Fractures and Epiphyseal Dislocations, New York, Paul B. Hoeber, 1917, p. 111; Report on a Case of Birth Dislocation of the Lower Femoral Epiphysis, Bull. Lying-In Hosp. **9**:327, 1914.

Case 2 (Massart [5]).—A boy was born at full term, by breech delivery. The accoucheur informed the parents that swelling of both thighs was present at birth. Labor was difficult and lasted thirty-six hours. Massart saw the baby when it was 30 days old. Both thighs near the knees were swollen in the form of cones with distal bases. Palpation of the swollen thighs was painful. Flexion of both knees was complete, but extension did not go beyond 90 degrees. A roentgenogram taken at the age of 18 days showed the distal epiphysis of each femur to be placed posteriorly in the lateral view but centrally in the antero-posterior view. The displacement was of no great degree but was more marked on the right side. The periosteum of each femoral shaft was stripped for three fourths of the length of the bone. Subperiosteal ossification was wider distally. In the belief that the lesion was syphilitic, the baby was given mercurial treatments despite the fact that the mother's Wassermann reaction was negative. At the age of 10 months there was no increase in the volume of the femur. Motions of the knee were full. There were no signs of syphilis.

Case 3 (Pincherle [6]).—The mother, a primipara, was delivered of her baby in podalic presentation with the aid of a midwife. During the delivery the baby's legs were flexed at the knees and the thighs flexed at the hips. The midwife said she used no traction on the limbs. Pincherle saw the child when it was 14 days old. The child did not move the lower extremities spontaneously, and passive motion of the knees was limited and painful. Both knees were swollen, and the swelling extended to above the supracondylar region of the femur. The exact time of onset of the disability was not known to the parents. A roentgenogram taken at the age of 11 days showed posterior displacement of both lower femoral epiphyses. There was extensive subperiosteal stripping of the femoral periosteum, and a great deal of subperiosteal ossification was present. At the age of 3 months it was noted that the epiphysis of each side was in proper position and that the periosteal new bone was in regression. There was remodeling of the shaft. The lower third of the femur was angulated in such a manner that the epiphysis was brought under it. It was also broadened. Conservative therapy was used. Both lower extremities were first put in traction and successive casts were then applied, each one bringing the knee into more extension. The casts were discontinued at the age of 2 months, and at this time motion of the knees was free and painless. A fusiform thickening of the lower end of the femur still remained.

Case 4 (Our Own Case).—A primipara was delivered of a boy by breech presentation on Aug. 2, 1936, at the Flushing Hospital in Queens. The baby weighed 6 pounds and 7 ounces (2,948 Gm.). Within the first three days it was noted that the left lower extremity was limp and that the region of the left knee was swollen. A roentgenogram taken August 5 (fig. 1) showed a posterior and lateral displacement of the distal femoral epiphysis. Manipulation of the knee without anesthesia was tried by Dr. Langsam at the age of 3 days. This was not successful. Another manipulation was tried at the age of 7 days, with the baby under ether anesthesia at the Flushing Hospital, by Dr. Burman. This was done under fluoroscopic control. The joint space was widened medially by putting the knee into 45 degrees of valgus and into full flexion, downward and

5. Massart, R.: Décollement epiphysaire de l'extrémité inférieure des deux fémurs consecutif à un traumatisme obstétrical, Bull. Soc. anat. de Paris **18**:498, 1921.

6. Pincherle, B.: Distacco epifisario inferiori bilaterale del femore da trauma ostetrico, Pediatria **44**:816, 1936.

lateral pull being made on the epiphysis. This was done to provide a space for the reception of the epiphysis anteriorly. This part of the maneuver increased the deformity by mobilizing the epiphysis. The epiphysis was then pulled anteriorly and medially, and at the same time the knee was extended and put in about 5 degrees of varus to lock the epiphysis in its new position. The knee, however, could not be completely extended even with the baby under anesthesia. A hip spica was then applied. This procedure was only partly successful because of the fixity of the epiphysis. The inability to reduce the epiphysis completely was verified by roentgenograms taken immediately after the procedure.

The baby was admitted to the Hospital for Joint Diseases on August 13, when he was 11 days old. His general health was excellent. The left knee was swollen and showed a flexion deformity which prevented extension beyond 90 degrees. Flexion was full and painless from this limited position of extension. The knee was held in about 20 degrees of valgus but could be passively abducted to 45 degrees. The configuration of the knee was altered so that the upper, or femoral, part seemed more anterior, while the lower, or tibial, part seemed more

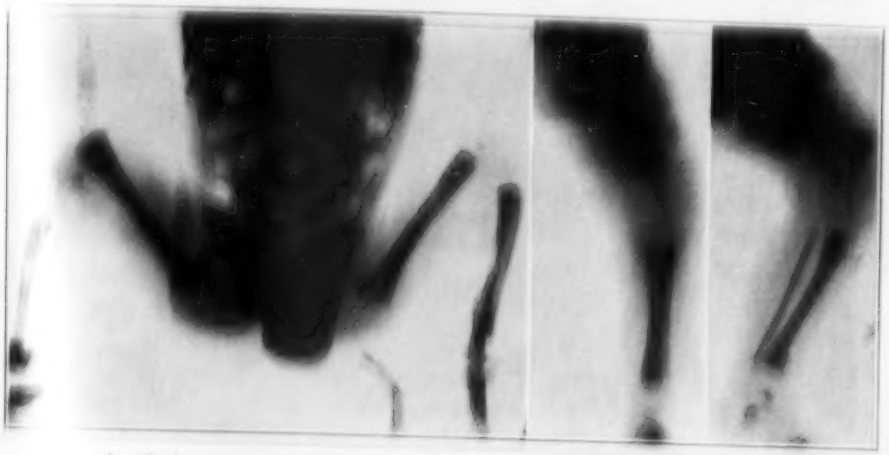

Fig. 1.—Left, roentgenogram of August 5, taken when the child was 3 days old. There is no subperiosteal calcification as yet. The distal femoral epiphysis is displaced posteriorly and somewhat laterally. Right, roentgenogram of August 10, eight days after birth. Subperiosteal ossification, which is greatest posteriorly and widest at the base of the epiphysial line, extends about halfway up the shaft of the femur.

posterior. Most of the swelling was on the medial side of the lower end of the femur. The skin at one point medially was dead white and surrounded by a zone of bluish discoloration the size of a dime, as if the underlying and anteriorly placed femur were about to perforate the skin by pressure necrosis. The left knee measured 6 inches (15 cm.) at the point of greatest swelling; the circumference of the right knee with the knee held in similar position was 4½ inches (11.3 cm.). With the knee in the flexion position there was a marked side to side movement, a little more than in the normal right knee. Manipulation of the knee seemed to be painful.

A roentgenogram taken August 10 (fig. 1) showed a marked posterior and a lesser lateral displacement of the lower femoral epiphysis, as indicated by the position of its oval center of ossification. There was an extensive subperiosteal hemorrhage which extended a little more than half way up the shaft of the femur.

The area of subperiosteal ossification was widest near the lower femoral epiphysis and greatest posteriorly and laterally; the lines of the shaft of the femur were clearly visible.

In view of the failure of manipulation, open reduction of the displaced epiphysis (by Dr. Burman) was resorted to on August 15 with the baby under general anesthesia. The Esmarch bandage and tourniquet were used to make the operative field bloodless. The joint was opened by the usual median parapatellar incision. This incision was used rather than any other because the lower femoral epiphysis is a part of the knee joint. The quadriceps muscle was diffusely edematous, pale and friable; it was hemorrhagic in occasional areas. The tendon of the quadriceps could not be clearly defined, and an incision was made through the muscle substance in the line of the cutaneous incision. A small amount of clear fluid escaped when the joint was opened. The lower end of the femur, which was red and beefy, was displaced anteriorly and medially. The entire lower femoral epiphysis was dislocated, and no part of the epiphysial plate was attached to the stump of the femoral shaft. The epiphysis was placed posteriorly and somewhat laterally, and a little upward (proximally) behind the shaft of the femur. The epiphysis was tilted obliquely in valgus of 20 degrees, with no particular rotation of the epiphysis, although its medial end seemed a little more anterior than its lateral end. Its condyles were perfectly formed and were an integral part of the knee joint. The meniscuses were not examined. The anterior and posterior crucial ligaments were normal. A little of the grayish tissue of the epiphysial plate was seen anteriorly and proximally, as if it had been squeezed out. The epiphysis was fixed firmly by scar tissue so that it could not be moved by the moistened, gauze-covered finger or by a skin-towel clip. The adherent tissue was carefully dissected away, especially posteriorly and laterally. To mobilize the epiphysis it was necessary to cut the internal lateral ligament at its point of origin. In dissecting away the adherent posterior portion of the capsule, close dissection was necessary to avoid the popliteal artery. A superficial flake of cartilage was cut away posteriorly. After this dissection had been done, it was easy to mobilize the epiphysis and to put it into its normal position, light lateral pressure being made on the lower end of the femur. A thin tongue of bone was present on the anterosuperior and lateral part of the epiphysis. A suture was placed through this tongue of bone and through muscle; when the suture was tied, the epiphysis was kept snugly in place. Another suture was taken medially through the point of origin of the internal lateral ligament and through muscle; after this suture was tied the ligament was taut, and the lateral instability of the knee was overcome. The wound was closed in layers, suturing being a little difficult because of the friability of the tissues. Configuration of the knee was restored after reduction. The knee was immobilized by a hip spica of plaster of paris, the knee being held in full extension and in 5 degrees of varus. The foot was placed in plantar flexion to relieve any strain on the back of the knee.

The postoperative course was uneventful, and the wound healed by primary intention. The baby was bottle fed by an appropriate formula. A postoperative roentgenogram showed that there was still some displacement of the epiphysis, indicating slipping of the epiphysis during the application of the cast. A roentgenogram (fig. 2) was taken when the cast was removed, just before manipulation. The lateral view showed the epiphysis still posteriorly placed but to a lesser degree than before operation; the anteroposterior view showed a lateral displacement of the epiphysis. Subperiosteal ossification was more evident and was especially marked posteriorly and laterally.

The knee was manipulated without anesthesia, under fluoroscopic control, on August 20. The epiphysis was movable, and only with the knee in extension could it be made to approximate its normal position. With the knee in flexion it slipped posteriorly. The epiphysis was easily displaceable. A hip spica was again applied after the epiphyses had been normally placed. Because of the easy mobility of the epiphysis, however, it could not be made certain that the

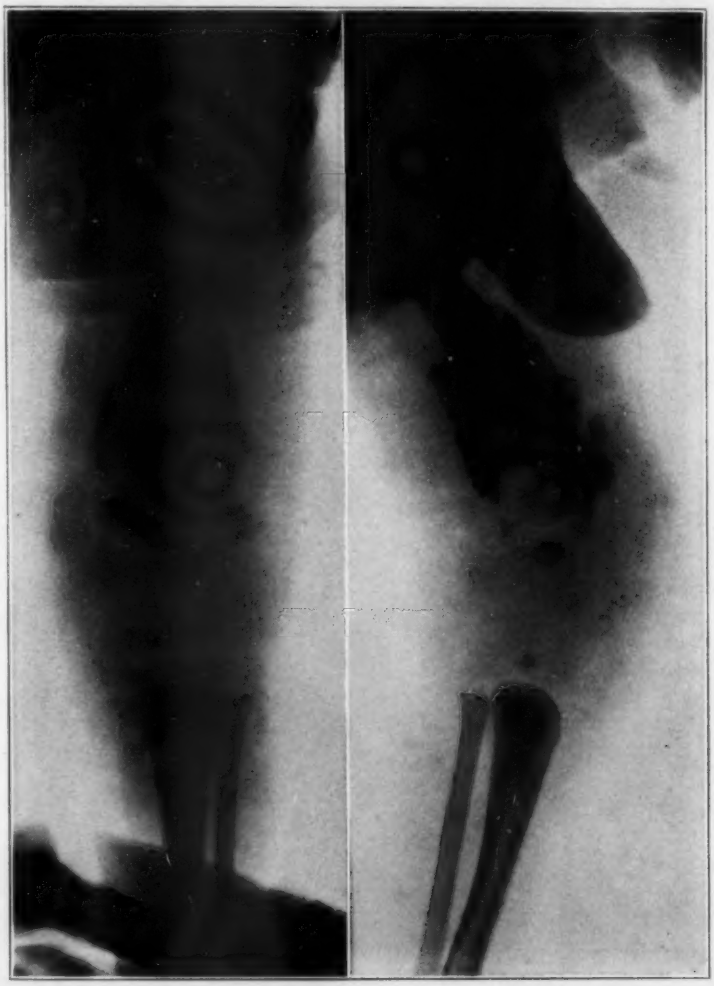

Fig. 2.—Roentgenograms of August 20, five days after open reduction of the displaced epiphysis. The epiphysis is still placed posterolaterally, but in the anteroposterior view there is beginning central placement of the epiphysis by an increase in the subperiosteal bone laterally.

exact placement of the epiphysis had been maintained. The roentgenogram of August 26 showed central placement of the epiphysis in the anteroposterior view but still some posterior displacement in the lateral view. The plaster was wedged at the knee joint to increase extension. On September 10 the hip spica

was removed. The alinement of the knee seemed good, but there was still some anterior prominence of the lower end of the femur. The femoral shaft was thickened in its lower third. A deep crease was present at the upper part of the tibia, and it was in this region that most of the effect of the wedging

Fig. 3.—Roentgenogram of September 10. The epiphysis is now placed centrally. A greater amount of subperiosteal bone, which has formed posteriorly and laterally, has broadened the shaft so that it covers the epiphysis. The femoral shaft shows an anterior convexity which is due to posterior bending of the lower part of the shaft, its purpose being to meet and cover the displaced epiphysis. The lines of the femoral cortices are less distinct.

had taken place, although the site of wedging had been verified by roentgen examination to be at the knee joint proper. Extension was 165 and flexion 145 degrees. Wedging of the cast had been ineffective on the displaced epiphysis.

The roentgenogram of this date (fig. 3) was instructive. The lower half of the femoral shaft was much wider than usual because of the great amount of subperiosteal bone. The cortices of the femur were losing their distinctness and being gradually absorbed. The epiphysis was centrally placed in both the anteroposterior and lateral views. This had been accomplished by the new periosteal bone, which had grown so as to place the epiphysis centrally. There

Fig. 4.—Roentgenogram of November 7. The epiphysis is centrally placed in both the lateral and the anteroposterior view. The shaft has been remodeled, and the lines of the cortices of the femoral shaft are gone.

was more new bone formation posteriorly. In the lateral view the lower end of the femur was hollowed, but in the anteroposterior view it was straight. The lines of the femoral condyles were not distinct.

A long leg cast was applied with the knee held in extension. This cast was removed on October 3. The child was examined periodically. On November 7

extension was 175 and flexion 80 degrees. The right lower extremity (anteriorly) measured 9¼ inches (23.5 cm.); the left lower extremity (anteriorly), 9⅜ inches (23.8 cm.). The circumference of the right thigh was 6⅜ inches (16.2 cm.), and that of the left thigh, 6¾ inches (17.1 cm.). The legs seemed equal in length, and the external configuration of the knee was normal. The roentgenogram of that day (fig. 4) showed central placement of the epiphysis. Almost total remodeling of the femoral shaft had taken place. The cortices of the shaft could just be seen. The new shaft was wider than normal, showed an anterior convexity and was a compound of the old shaft and the new periosteal bone. The lower end of the femur was hollowed opposite the center of ossification of the epiphysis, and the lateral femoral condyle was more pronounced than the medial.

On Feb. 27, 1937, the child was about 7 months old. Extension was about 175 degrees, and flexion was complete. There was no lateral or medial deviation of the knee. The length of both lower extremities was 10¾ inches (27 cm.).

Fig. 5.—The two left films were taken May 22, 1937. This lateral view shows both the normal right knee and the left knee. The femoral shaft is completely remodeled and is somewhat atrophic. The epiphysis is centrally placed and equal in size to that of the right knee. On the right are anteroposterior views of the knees, of the same date. The left femoral shaft has been completely remodeled. It is atrophic and a little narrower distally. The epiphysis is centrally placed, but the epiphysial line is slightly irregular and is tilted upward and medially.

On May 22, 1937, at 9 months and 25 days of age, the baby still showed a mild thickening of the lower end of the femur. Both lower extremities were 11⅝ inches (29.5 cm) in length. The circumference of the right thigh was 8¼ inches (20.9 cm.) and that of the left thigh 8½ inches (21.5 cm.). Flexion was complete. There was no lateral instability of the knee. The contour of the knee was normal. The patella was normal in shape and normally movable. Both legs were slightly bowed. A roentgenogram of this date (fig. 5) showed some atrophy of the now completely remodeled shaft. The distal end of the bone was a little narrower than that of the normal right femur. The epiphysis was properly placed, but it was tilted slightly upward and internally by a medial obliquity of the slightly irregular epiphysial line.

The child was last examined fourteen months after operation. He walked well. The angle of greatest extension was still 175 degrees, flexion of the knee being complete. The knee showed no lateral instability. There was now shortening of ½ inch (1.2 cm.).

The roentgenogram showed no irregularity of the epiphysial line, but the epiphysis was still tilted obliquely so that its medial end was more proximal than its lateral end. The epiphysis was centrally placed. There were slight fuzziness and fragmentation medially and superiorly, suggesting an osteochondritic change. The lower end of the femur was bent posteromedially. The posterior surface of the distal part of the femur, just proximal to the epiphysial line, was somewhat irregular. A line of increased bony density was noted, running from the middle of the distal part of the femoral shaft obliquely, proximally and laterally to end about 1 inch (2.5 cm.) above on the lateral side of the distal part of the shaft.

COMMENT

Posterior dislocation of the lower femoral epiphysis is a birth injury conditioned by severe trauma during prolonged delivery by breech presentation in primiparas. This dislocation is the reverse of the usual anterior (cartwheel type) dislocation of this epiphysis in adolescents. The attachment of the two heads of the gastrocnemius muscle tends to pull the epiphysis posteriorly after it has been separated. The femur was not fractured in any of the living babies. The deformity, then, is a flexion deformity of the knee, with more or less valgus of the knee, conditioned by the epiphysial displacement in valgus.

The sex of the babies was mentioned in only 2 cases. Both infants were boys. The swelling of the knee joint and of the femur adjacent to it was noted at various times after delivery—immediately, within two days and presumably later. The involved lower extremity was limp, and the passive motions of the affected knee were painful. There was no reason to suspect an infection of the thigh since the soft tissues were not red or hot.

The epiphysial injury was unilateral in 2 cases and bilateral in the other 2. Such an injury is invariably accompanied by severe subperiosteal stripping, with early ossification of the hemorrhage. This develops quickly. It is seen already to be advanced in roentgenograms taken from eight to eighteen days after birth. The subperiosteal hemorrhage may be more severe than the epiphysial dislocation, as in Massart's case. It is this periosteal new bone which alters the shape of the femur and by its greater formation posteriorly and sometimes laterally tends to place the epiphysis centrally again. The lower part of the femur usually bends posteriorly to meet the displaced epiphysis. This produces an anterior convexity of the distal femoral shaft. This happens no matter what form of treatment is given. A period of two or three months elapses before the central placement of the distal epiphysis is completed.

Since nature itself remedies the defect, only the simplest treatment need be given, either traction or a cast holding the knee extended. In Massart's case, no treatment was given beyond mercurial rubs. In Truesdell's case the limb was bandaged in flexion, a position of the knee which increases the deformity; yet in both cases good results were obtained by the remodeling of the shaft of the femur. Within a few months the shaft is remodeled and the epiphysis centrally placed. Remodeling of the shaft of the femur begins after five to nine weeks. This is complete within a period of nine months, although in 1 case it was almost complete when the child was 9 weeks of age. Manipulation or open reduction is not indicated, and this is not refuted by our own experience. There is, however, a great temptation to try these measures.

The time for restoration of function is variously estimated between the ages of 2 and 10 months. In 1 case it was noted that motion of the knee was free and painless at the age of 2 months. In another, at 6½ months there was still slight restriction of extension. The baby in our case showed restriction of extension of 1 or 2 degrees when almost 14 months of age. The prognosis is excellent for useful function of the injured part.

The extent of damage sustained by the epiphysial plate is problematic. In no case is the answer in terms of shortening or deformity given. In our case, which has the longest follow-up, there is an upward and inward inclination of the epiphysial line. Resultant deformity may or may not develop, but theoretically it is probable.

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ENDOMETRIOSIS

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Endometriosis, or adenomyoma, does not occur frequently as a clinical entity. However, it can no longer be regarded as a pathologic curiosity. Cullen in 1,283 cases of myoma found adenomyoma in 73, or 5.7 per cent. MacCarty and Blackman at the Mayo Clinic reported a series of 3,398 cases of fibromyoma, in which 211, or 6.4 per cent were instances of endometriosis. Tyrone reported similar statistics. Sampson reported 332 laparotomies, with endometrial implants in 98 or 29 per cent. This percentage is high, but endometriosis is his specialty and he has constantly been looking for these lesions. His classic work has established endometriosis as an important condition. Statistics show that in the majority of cases the condition is undiagnosed before operation. With this point in mind, I reviewed the literature and analyzed the cases of endometriosis observed at the St. Francis Hospital and the Sedgwick County Hospital from 1931 to 1937 with the hope of reemphasizing the causes, diagnosis and treatment of endometriosis. I was able to collect 29 cases.

The term endometriosis has been defined by Novak as that condition in which endometrial tissue occurs aberrantly, that is, outside of the uterine cavity. This definition is broad, for it includes conditions in which the uterine musculature is invaded, as in Cullen's adenomyoma; Bell's adenomyosis; Bailey's endometrioma; mullerianoma; chocolate cysts, and tumors of the inguinal canal or of the umbilicus.

The various locations of endometriosis are well illustrated by Cullen's diagram (fig. 1). In this series of 29 cases there were 19 in which the condition was intrauterine and 10 in which it was extrauterine. The extrauterine lesions were located as follows: in the ovaries, 3; in old scars, 2; in the sigmoid flexure of the colon, 1; in the inguinal canal, 2; in the umbilicus, 1; in the tubes, 1.

Sites of the lesion in other series are given in the accompanying table.

ORIGIN

There is a difference of opinion as to the mode of origin of the various endometrial lesions. It is difficult to find one theory that satisfactorily explains such tumors. The first case of adenomyoma of the uterus was reported in 1860 by Rokitansky. Chiari described several cases in 1867 and said the condition was due to inflammation, such as

salpingitis or postabortal infection. Later (1896) von Recklinghausen reported cases of adenomyoma in which the condition was due to the embryonic rest from the wolffian system or mesonephron tissue. The presence of tumors in the pelvis and groin was thought to be the result of extension of the gubernaculum ovarii to the groin through the round ligament or canal of Nuch. This theory was superseded by

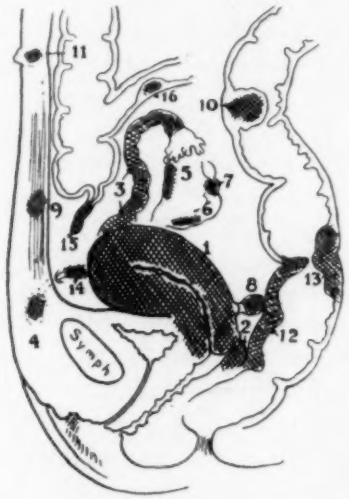

Fig. 1.—Sites at which endometrial lesions are found. This drawing illustrates the fact that no one theory has explained satisfactorily the origin of endometriosis. (After Cullen.)

Location of Endometrial Lesion

Location	King (70 Cases)	Keene (113 Cases)	Clark (29 Cases)
Uterus	17	0	19
Ovary	23	110	3
Tube	4	0	1
Peritoneum	26	0	0
Laparotomy scar	0	1	2
Umbilicus	0	2	1
Inguinal canal	0	0	2
Sigmoid	0	0	2

Cullen's invasion theory. In 1898 he definitely proved by serial microscopic slides that there is a communication between the gland spaces of the tumor and the uterine mucosa. In the same year, Ivanoff suggested the theory that endometriosis is a result of metaplasia of the peritoneal endothelium. The question is what causes the metaplasia. Witherspoon and Novak believe it is initiated by estrogen. In 1899 Russell reported the observation of endometrial tissue in the ovary and attributed its origin to aberrant portions of the mullerian ducts. Cullen agreed with this theory for extrauterine adenomyoma, and this is still

one of the most plausible theories. In 1903 Robert Meyers declared that endometriosis is the result of miliary abscess in the muscle wall of the uterus with ingrowth of the endometrial glands between the muscle fibers, supporting Cullen's invasion theory. The first case report in this series supports this theory. Meyer's theory is applicable to extrauterine growths, because the germinal epithelium of the ovary may undergo transformation into cylindric epithelium which microscopically resembles endothelium or uterine mucosa. Hertzler says this is expecting too much from the peritoneum.

In 1906 Sitzenberg published the theory that endometriosis is the result of proliferation of endothelial cells from the lymph channels. This theory was not recognized.

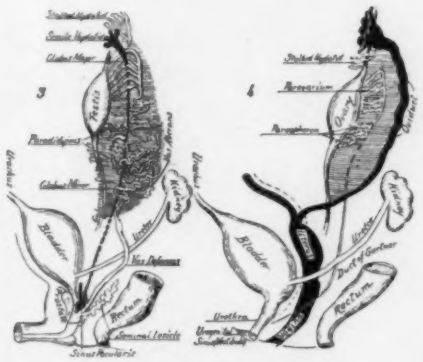

Fig. 2.—Diagrammatic sketch illustrating the many possibilities of the embryonic rest theory of endometriosis in the ovary and groin.

Sampson in 1921 published his implantation theory—that the menstrual endometrium is regurgitated through the tube into the peritoneal cavity, and in a suitable environment these endometrial cells develop into endometrial growths. The objection to this theory is that menstrual endometrium is not living tissue, and a chemical irritation would cause closure of the tube. It must be admitted that the endometrial growths occurring in scars after operation on the uterus or tubes (fig. 3) support this theory, but this endometrium is living tissue brought through by needle and suture. Jacobson's experimental work on transplantation of endometrial tissue in the rabbit also supports this theory. However, Hein was unable to produce the same lesion in the monkey, and the theory seems contrary to the principles of embryology and pathology.

Novak supported the theory advanced by Ivanoff and called attention to the origin of genital epithelium and peritoneum from the celomic

mesothelium. He concluded that metaplasia is due to endocrine stimulation, since it has been proved that estrogen influences the whole genital tract, as is illustrated by treatment of vaginitis by estrone (theelin).

These theories have been listed to give an idea of the vast amount of work that has been done on endometriosis. No one theory entirely satisfactorily explains the origin of the different lesions.

Fig. 3.—Endometriosis in a laparotomy scar after a suspension operation four years previously. Note the areas of miniature uteri.

PATHOLOGIC PICTURE

The gross picture of endometriosis varies. There may be small areas of glands causing no symptoms, or there may be extreme cases in which the whole pelvis is filled with adenomyomatous invasion involving the sigmoid flexure and the rectovaginal septum, simulating a malignant tumor. The uterus is usually two or three times the normal size and is symmetrically enlarged, with tiny cystic areas scattered throughout the muscle wall. These cystic areas are dark brown, almost purple-

mulberry color, and contain blood, which at the time of menstruation finds its way to the uterine cavity; or if the growth is extrauterine it enlarges and causes more pain from distention of the miniature uteri.

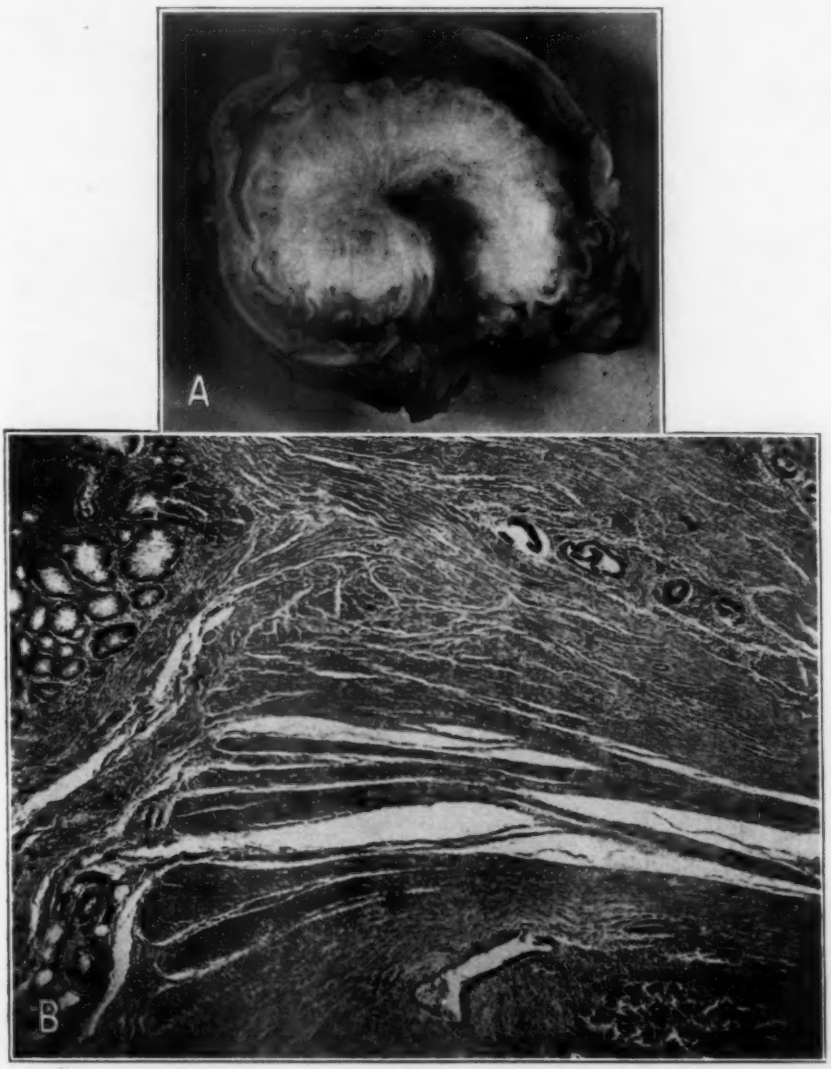

Fig. 4.—*A*, endometrial tumor in the wall of the sigmoid flexure of the colon, causing obstruction and death. *B*, high power microscopic section of the specimen *A*. Note the gland in the sigmoid and the areas of endometrial tissue.

Microscopically such a tumor consists of fibrous connective tissue and smooth muscle fibers. There are glandular spaces lined with cylindric epithelium like that in the uterine mucosa. These glands are

embedded in cellular stroma which is like that lining the cavity of the uterus, so that the tumor is similar to a miniature uterus. There is always evidence of hemorrhage or menstruation, and there are often wandering cells or clasmatocytes picking up the old blood cells (fig. 5).

SYMPTOMS

Endometriosis presents an interesting problem in differential diagnosis, well illustrated by the first case reported here. The patient in this case was treated for several different conditions by eight physicians over a period of four years, without relief. The condition is often puzzling and difficult to handle. One author reported a case in which curettage had been done twelve times in eighteen years. The condition was finally cured by a hysterectomy.

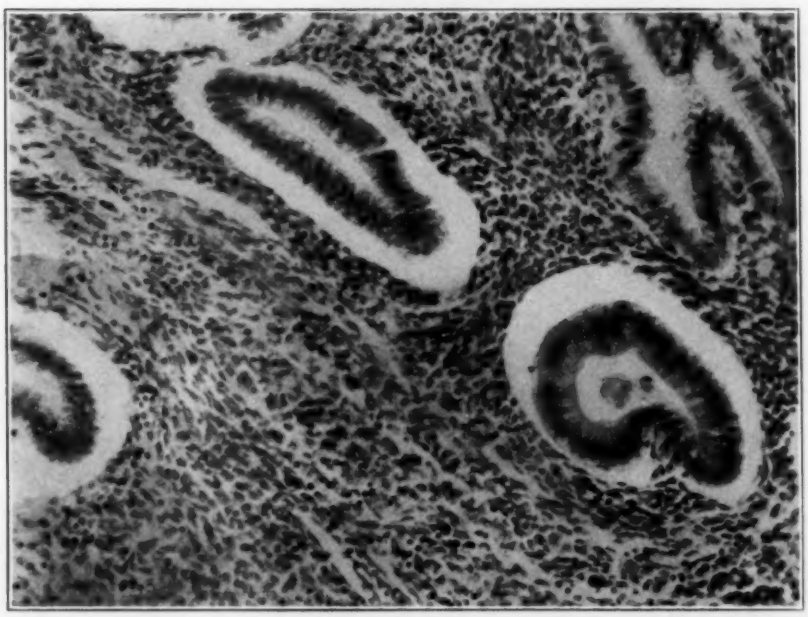

Fig. 5.—High power microscopic section of endometrial tissue in the groin. Note the miniature uteri with the endometrium in the engorged state and the clasmatocytes picking up the old hemosiderin.

The symptoms and diagnosis depend entirely on the location and extent of the endometrial lesion. Undoubtedly, many lesions cause no symptoms and are not diagnosed until operation. In many cases a history of dilatation and curettage, abortion or infection may be a predisposing factor and may help in making a tentative diagnosis. Endometriosis often gives a picture similar to that of chronic inflammation of the pelvis and cannot be diagnosed until operation.

The lesion develops usually after the age of 25 and rarely after 60. In this study the youngest patient was 23 years old and the oldest 62.

Pain is the most constant symptom. It may be intermittent at first, but later it is more or less constant. In this series pain was present in every case, and in many instances the pain was referred to the rectum.

Dyspareunia, as with other pelvic conditions, is a common symptom.

Dysmenorrhea is a common complaint and usually comes on after the thirtieth year of life, becoming more severe with each period and sometimes associated with nausea and vomiting.

The menstrual history depends on the extent of the lesion. The periods become prolonged until there is more or less constant menorrhagia and metrorrhagia. Some patients with endometriosis are sterile, although 65 per cent of MacCarty and Blackman's patients had borne children and 38 per cent of the patients in this study had borne children. It is because of this menstrual disorder that Novak believes the cause to be an endocrine stimulation.

Many patients complain of vesical and rectal symptoms, and of course these symptoms should be investigated by special methods of examination.

The physical findings vary in relation to the pathologic condition present. Halban's sign is usually present—that is, enlargement of the uterus or ectopic tumor premenstrually and a return to normal after the flow subsides. This is due to the glandular stroma, which undergoes the same cyclic changes as normal endometrium. All of these symptoms are present in other pelvic conditions, but a careful correlation of the facts suggests endometriosis in many cases in which the lesion otherwise might not be diagnosed until a radical operation has been done for a suspected malignant tumor and the tissue has reached the pathologist.

TREATMENT

Since endometriosis occurs during the period of child bearing it is desirable to preserve ovarian function. It must be remembered that the tumor reacts to ovarian stimulation and in all cases is cured by castration. The treatment is conservative surgical management for the particular case. As has been pointed out, some such lesions cause no symptoms, but if they were allowed to develop, symptoms would probably appear. Small lesions are best treated with electric cautery and watched for recurrence. When the tumor involves the uterus a supravaginal hysterectomy gives the best results. When the growth involves other pelvic structures complete surgical removal gives the best results and would no doubt be considered a conservative procedure. The tumors regress after removal of the ovarian stimulation, but one must consider the acute

menopausal symptom and govern treatment accordingly. Many have reported pregnancies after conservative treatment of endometrial growths.

Roentgen therapy and radium therapy have been advocated by Bowing at the Mayo Clinic, but this would produce a cure only by completely destroying the ovaries, and I believe surgical intervention to be more conservative treatment, with a possibility of removing the growth and saving part of a functioning ovary.

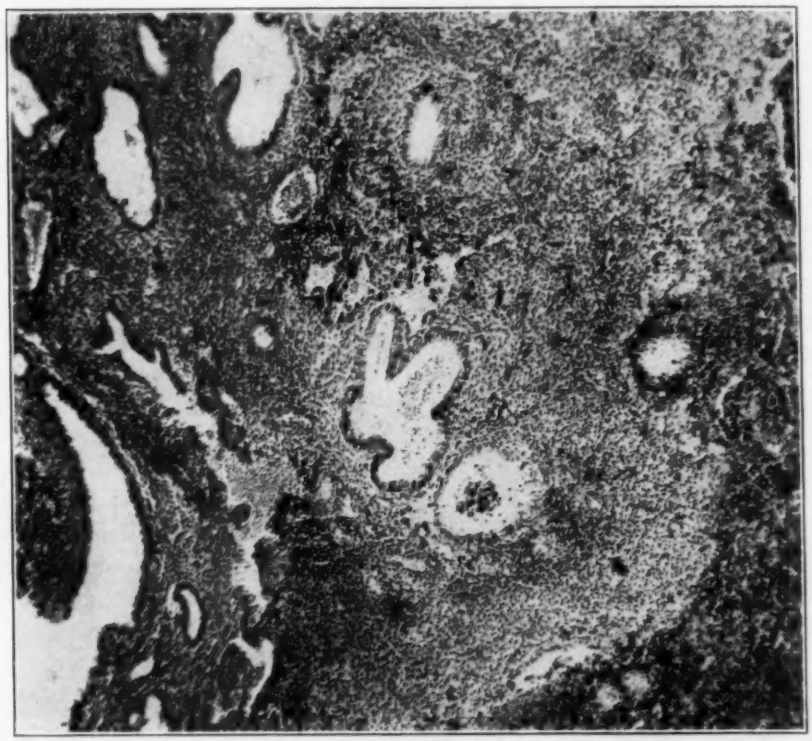

Fig. 6.—Endometrial scraping after an abortion. The diagnosis was suppurative endometritis. Note the typical uterine glands infiltrated with leukocytes.

REPORT OF CASES

CASE 1.—A woman aged 20 was referred to me on Nov. 20, 1934. She had had an induced abortion one year before and had had more or less flowing most of the time since. She could not differentiate a normal period. There had been severe pelvic pain and backache. For the last two weeks the patient had been in bed because of increased flowing and clots. The past history was irrelevant. The menstrual history began at the age of 11. The menses were painful and lasted three or four days. Her physician had tried many bottles of ergot and also dilation and curettage and many hypodermic injections of endocrine products, without results.

Physical examination gave essentially negative results. The temperature was 98.6 F.; the pulse rate was 96; the blood pressure was 100 systolic and 44 diastolic. The hemoglobin content of the blood was 66 per cent, and the erythrocyte count was 3,100,000. The vagina was normal. The cervix showed good position and was freely movable. The uterus was normal in size and position.

The diagnosis was incomplete abortion. I advised curettage, which was done November 20. The patient made an uneventful recovery. She was discharged November 25.

Pathologic Report on Endometrium.—The mucous membrane of the uterus was partly necrotic and heavily infiltrated with leukocytes, lymphocytes and plasma

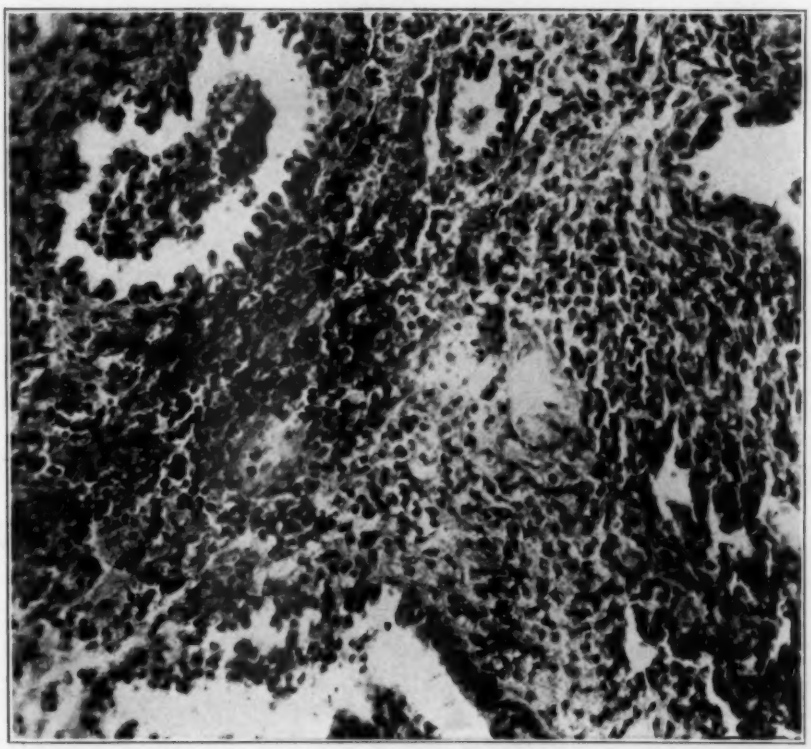

Fig. 7.—High power photomicrograph of the specimen in figure 6, showing areas of necrosis and inflammatory cells.

cells. The blood vessels were enormously dilated. The glands were wide and tortuous like those one sees in pregnant women. There was no definite placenta tissue. The diagnosis was acute suppurative endometritis; so I felt the symptoms were caused by chronic pelvic inflammation (figs. 6 and 7).

The bleeding continued in spite of ergot preparations and endocrine therapy. Consultation was held, and it was decided to use roentgen therapy to stop this functional bleeding. The patient received an enormous amount. She moved to a neighboring town. She was again given roentgen therapy and many injections of endocrine substance to stop the continued bleeding. At times it would cease for weeks; then the period flow would be excessive and would last two or three

Fig. 8.—Small uterus removed after roentgen therapy. Note the dark areas of endometrial tissue in the muscle wall.

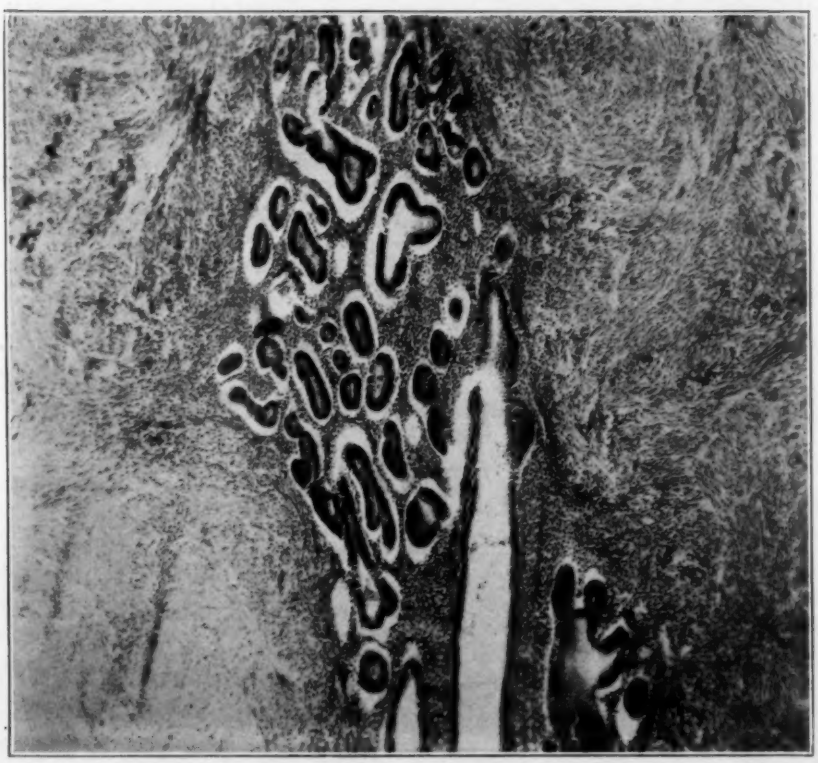

Fig. 9.—High power magnification of the specimen shown in figure 8. Note the islands of endometrial tissue, or miniature uteri.

weeks. She returned to me on Oct. 16, 1937, complaining of pain and continued flowing. Physical examination revealed a small uterus, freely movable. I considered a polyp and even a low grade malignant tumor of the body of the uterus. A diagnosis of endometriosis was considered, but the fact that the ovaries had been destroyed by the roentgen rays made me decide on a hysterectomy.

Supravaginal hysterectomy October 18 revealed a small uterus. The ovaries were the size of navy beans. The patient left the hospital free from symptoms of four years' standing.

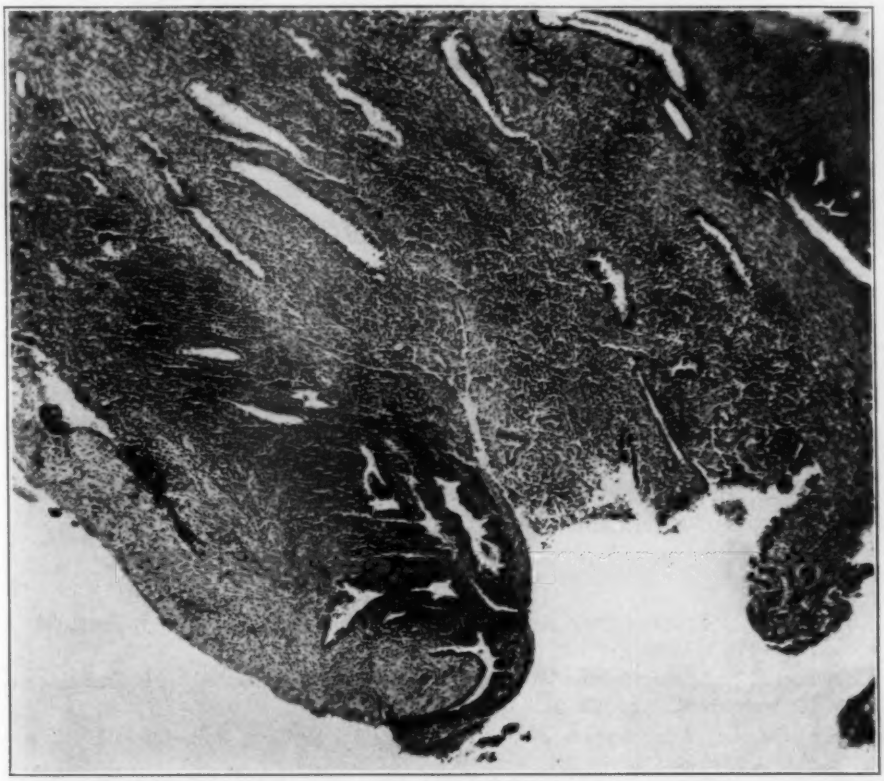

Fig. 10.—Microscopic section of a cyst wall, showing areas of endometrial tissue. Such cysts usually rupture, pouring their contents, which are intensely irritating, into the peritoneal cavity, thus involving other organs.

The pathologic diagnosis was adenomyoma or endometriosis of the uterus. This case supports Meyer's inflammatory theory because of the pathologic condition found in 1934 (figs. 8 and 9).

Case 2.—A white woman aged 25 entered the hospital complaining of severe pain, profuse menses and urgency and frequency of urination since an operation for the same symptoms in 1933. The uterus was partially fixed in the pelvis. The left ovary was the size of a tennis ball and was fixed to the bladder. At operation the condition of this ovary was seen to be typical of endometriosis, and the uterus showed areas of infiltration with small purple cysts.

After removal of the pathologic tissue the lumbar plexus was resected, and the patient left the hospital free from pain and symptoms.

The condition in this case can be explained by Novak's theory, as due to endocrine upset.

CASE 3.—A woman aged 46 complained of a small tumor at the umbilicus that became sore each month. A bloody discharge came from the umbilicus.

The diagnosis was clinical endometrioma.

A physician told her the condition would subside after the menopause; I am unable to verify this diagnosis with a microscopic section, but such tumors have been removed and typical endometrial tissue has been found to be the cause of the symptoms.

This case supports the metaplasia theory, and certainly the theory of origin in the wolffian system or in the mullerian ducts or the Sampson theory would not explain endometrial tumors of the umbilicus.

SUMMARY

The pathologic picture of tissue with histologic and functional characteristics similar to those of endometrium has been known since 1860, and yet many physicians are unfamiliar with the clinical entity. Various theories as to the origin of such lesions have been discussed, but no theory is satisfactory.

The symptoms depend on the extent of the lesion. However, pain, dysmenorrhea and irregular menstrual history, correlated with certain physical findings, strongly suggest an endometrial lesion. Early diagnosis will frequently obviate the necessity for extensive radical operation. The treatment of endometriosis is conservative operation.

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LEIOMYOSARCOMA OF THE URINARY BLADDER

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Sarcoma of the urinary bladder is an uncommon neoplasm, and leiomyosarcoma is even more uncommon. In a careful review of the literature we were able to find records of only 13 cases of leiomyosarcoma. The case to be reported here brings the total up to 14. It is possible that this list is not complete and that some cases may have been overlooked. Three cases, 1 reported by Albarran (1881) and 2 by Targett (1896), were referred to by Rabson; but, as he suggested, the evidence is insufficient for a positive diagnosis and hence they are not included in the present tabulation. Before discussing this subject in detail, we should like to report the following case.

REPORT OF A CASE

N. M., a man aged 55, single, was first admitted to the Presbyterian Hospital on Jan. 5, 1936.

The patient had had three attacks of gonorrhea, one of which was complicated by an attack of epididymitis on the left. A tonsillectomy was performed when the patient was 45 years of age and a herniorrhaphy on the right when he was 49.

The present illness began five years before the patient's first admission to the hospital. At the time of admission he complained of pain and burning on urination, frequency and urgency of urination, nocturia, difficulty in starting the stream, hematuria, backache and loss of weight. The symptoms were always aggravated by his becoming chilled or "catching cold," and they were definitely progressive.

The pain was present before and during urination and was referred to the glans penis. Burning occurred along the entire course of the urethra. Frequency of urination was so marked that the patient was finally obliged to urinate once every hour during both day and night. During the four years previous to admission he had four attacks of complete retention of urine, so that catheterization was necessary. The last time he had been catheterized was four months before his admission to the hospital, since which time all his symptoms had become much worse. One month previously he had had three attacks of hematuria. During the previous four months he had lost 35 pounds (15.9 Kg.) in weight. Replaceable rectal protrusions had been prominent for a year.

Physical examination showed an anemic, emaciated patient. The head and neck were normal; the teeth were carious and in need of repair. The heart, the lungs, the abdomen and the external genitalia were normal.

Rectal examination revealed large hemorrhoids which protruded on straining. The tone of the sphincter was normal. The prostate showed enlargement of grade 4

From the Presbyterian Hospital.

and was soft, smooth, elastic and slightly tender. No signs of carcinoma of the prostate were demonstrable.

The electrocardiogram showed ventricular extrasystoles and left axis deviation. A blood count showed: erythrocytes, 4,250,000 per cubic millimeter; leukocytes, 6,000, and hemoglobin, 85 per cent. The blood pressure was 135 systolic and 85 diastolic. Chemical studies of the blood showed the nonprotein nitrogen content to be 35.7 mg.; and the creatinine content 1.0 mg. per hundred cubic centimeters.

Examination of the urine showed the presence of albumin, the absence of sugar and a count of 2,050 red blood cells per cubic millimeter. Cultures showed short chain streptococci. No tubercle bacilli were found.

In the phenolsulfonphthalein test the time of appearance was six minutes. The total excretion in ninety minutes was 75 per cent.

Roentgen examination showed absence of stone in the urinary tract.

Intravenous pyelograms revealed bilateral hydronephrosis. The cystogram showed apparently normal conditions.

Cystoscopic examination (January 6) (with the region under local anesthesia) was very painful. The capacity of the bladder was limited. A large tumor was present, which seemed to be more or less papillary; because of the size of the growth the base could not be accurately defined, nor was it possible to determine whether or not there was a pedicle. The ureteral orifices could not be seen since they were covered by the tumor. A cystoscopic diagnosis of papillary tumor of the bladder was made, and a piece was removed for histologic study. This resulted in a diagnosis of papillary carcinoma.

Four days later (January 10), with the patient under sacral anesthesia, bipolar fulguration of the tumor was done with the Stern-McCarthy resectoscope.

Examination with the resectoscope on February 22 showed a large tumor. Many necrotic areas were seen, which were the result of fulguration. Resection of large masses of the tumor and also fulguration were carried out at this time.

On February 29 a transurethral resection of the prostate was done with the patient under sacral anesthesia.

The histologic diagnosis of some of the removed pieces was benign adenoma of the prostate.

The resection was followed by acute prostatitis and periprostatitis. In addition, a tentative diagnosis of acute pyelonephritis was made, and the patient was discharged from the hospital on March 20.

On April 4 the patient was admitted to the hospital for the third time, because of increased frequency of urination and pain in the lower part of the sacrum. A diagnosis of acute exacerbation of the prostatitis was made. The patient was discharged.

Four days after the previous discharge (April 17) the patient entered the hospital for the fourth time. Profuse hematuria was present; the urine was very bloody, and many blood clots were passed. In addition to the hematuria he had severe urgency and frequency of urination, severe pain in the lower part of the abdomen and pain on urination. It was necessary to administer codeine every three hours. Since all attempts to control the bleeding were of no avail, it was decided to perform a suprapubic cystostomy.

On May 5 a suprapubic cystostomy was performed with the patient under ethylene anesthesia. The perivesical veins were unusually large, tortuous and dilated, and the vesical wall was enormously thickened. Examination of the interior of the bladder showed a large tumor that almost completely filled the entire

vesical cavity. A piece of the tumor was removed for biopsy. A total of 5,511 milligram hours of radium was given. The patient was discharged on June 25.

The histologic diagnosis of the tissue removed at operation was carcinoma of the bladder.

The patient was admitted to the hospital for the fifth time on August 2. He had been fairly comfortable until twenty-four hours before his fifth admission, when he was seized with a severe attack of pain in the chest, some shortness of breath and a mild cough. Great emaciation and severe anemia were present. Diagnosis was made of an infarct in the lung. The patient left the hospital in ten days.

Fig. 1.—Autopsy specimen. The tumor almost filled the vesical cavity.

Subsequently, severe pain developed in the lower part of the abdomen, especially in the region of the bladder and rectum. The pain was excruciating and practically continuous. No relief was obtained from 1 grain of morphine or a combination of 1 grain of pantopon (a mixture of the hydrochlorides of the opium alkaloids) with 1 grain of codeine. The urine was very bloody. Apparently there was bleeding from the tumor. On account of the severe, uncontrollable pain, Dr. A. Verbrugghen was called into consultation, and it was decided to perform a chordotomy in the hope of instituting relief.

On Oct. 8 a chordotomy was done by Dr. Verbrugghen. After the operation, the patient had a very stormy convalescence: high fever, pain in the kidneys, severe diffuse abdominal pain and marked abdominal distention occurred. A diagnosis of acute pyelitis and pyelonephritis was made. The patient died on October 15.

Autopsy was performed by Dr. Carl Apfelbach. The anatomic diagnosis was as follows: leiomyosarcoma of the urinary bladder, with extensive dilatation of the lumen and ulceration and gangrene of the wall; spontaneous perforation of the urinary bladder; severe bilateral hydronephrosis and hydroureter; suppura-

Fig. 2.—Low power photomicrograph of a leiomyosarcoma, showing spindle-shaped cells.

tive cystoureteropyelonephritis; two left renal arteries; acute generalized fibrinopurulent peritonitis; localized fibrous peritonitis; slight hyperplasia of the spleen; emaciation; anemia; chronic interstitial hepatitis; bilateral disseminated fibrous pleuritis; unhealed cystostomy wound; recent chordotomy; linear scars of the penile portion of the urethra; coal pigmentation of the lungs.

The capacity of the bladder was very large. The bladder was about twice the normal size. The vesical wall was greatly thickened; in some areas it was 3 cm. thick. The tumor was irregularly shaped and soft; a large part was discolored, the color varying from greenish brown to black; here and there

Fig. 3.—High power photomicrograph of a leiomyosarcoma, showing striations of the neoplastic cells.

it was white. Some of the tumor masses were pedunculated. The lining of the trigon and the prostatic portion of the urethra was grayish brown and firmer than normal (fig. 1).

TABLE 1.—*Basis for Diagnosis in Previously Reported Cases of Leiomyosarcoma*

Case	Year	Author	Microscopic Description	Comment
1	1875	Gussenbauer (Billroth)	"Spindle cells which could not be differentiated from organic muscle cells: myosarcoma: rich in smooth muscle fibers. Interstitial cells of sarcoma and carcinoma. Smooth muscle cells showed activity of multiplication and grew by cell division. Young cells round and odd but transition forms between these and typical smooth muscle cells."	
2	1885	Eve	"Mixed or myosarcoma: 3 classes of cells: (1) large cells with spheroid nuclei, epithelioid but of connective tissue origin; (2) young cells of above; (3) nucleus elongated, mitosis, in process of formation of unstripped muscle fibers. Hyperplasia of all elements except epithelial. New formation of muscle fibers not most marked feature."	Rabson stated the evidence insufficient to diagnose leiomyosarcoma
3	1888	Nicolich	"Predominating tissue is smooth muscle. A large part of these cells are round; others oval or irregular: of varying size: the nuclei of many are fusiform to round, enlarged. Diagnosis—myosarcoma."	
4	1895	Klein	"Large, wide, very long spindle cells, small central nucleus: stand out definitely: longitudinal striation but no cross striation: large smooth muscle fiber. Tumor same as polypous sarcoma occurring in the vagina."	
5	1904	Lexer	"True myosarcoma, as has been frequently operated."	Rabson stated the evidence insufficient to diagnose leiomyosarcoma; Henke and Lubarsch include this case in their list
6	1904	Röder	"Smooth muscle fibers, easily recognized through rod type nuclei and protoplasm which stains intense yellow with Van Gieson. Also cells without particular character so that tumor could be called a true myosarcoma."	
7	1927	Burlakov	"Structure corresponds to that of smooth muscle tissue. Polymorphous cells, sarcomatous: consists solely of smooth muscle fibers. Falls between leiomyoma and true sarcomas: a polymorphous sarcoma-like leiomyoma."	

TABLE 2.—*Tumors of the Urinary Bladder*

Author	Tumors of the Bladder	Sarcoma	
		Number	Percentage
Albarran	89	2	2.25
Caulk	303	1	0.33
Davis	41	2	4.88
Egger	83	1	1.20
V. Frisch	300	1	0.33
Fuchs	136	1	0.74
Gardner	369	6	1.63
Geraghty	180	2	1.11
MacKenzie	228	1	0.44
O'Niel	62	1	1.61
Pack and LeFevre	522	2	0.38
Rabson (cases by Stepita)	860	2	0.24
Scholl	262	1	0.38
Total	3,435	23	0.67

Histologic Stricture.—Sections of the neoplasm were fixed in Zenker's fluid and stained with hematoxylin-azure-eosin, Van Gieson's stain, phosphotungstic acid–hematoxylin and Foot's modification of Bielschowsky's stain. The characteristic cell in the neoplasm was a large spindle-shaped cell several times as large as the normal fibroblast. The cells were arranged in interlacing bundles, but the structure only slightly resembled the usual parallel arrangement of muscle cells (fig. 2). In a large part of the neoplasm necrosis and gangrene had occurred. Consequently, there were only a few regions in which the finer details of the cells were still present. The nuclei varied greatly in shape, size and chromatin content. Some of them had nucleoli. There were a few multinucleated cells. Mitotic figures were sparse, and in some of the neoplastic cells the fibrillar arrangement of the cytoplasm was demonstrated.

In Van Gieson preparations the cytoplasm stained light yellow. Argentophilic fibrils were present in small numbers. Collagenous fibers were more abundant. The striations of the neoplastic cells were best demonstrated in preparations stained with phosphotungstic acid–hematoxylin (fig. 3).

COMMENT

It is not our object to discuss the subject of sarcoma of the bladder in general, since this has been the subject of several recent papers, to which those who are interested may refer. We shall limit our remarks to leiomyosarcoma, except as it may be necessary to refer to the general topic of sarcoma of the bladder.

We are mindful of the fact that in some cases reported as instances of leiomyosarcoma the diagnosis has been questioned by subsequent authors. We are also familiar with the fact that some of the questionable cases have been accepted without reservation by other authors; for example, the case of Lexer. Rabson stated that the evidence was insufficient to establish the diagnosis of leiomyosarcoma, whereas Henke and Lubarsch included this case in their list. Because of differences of opinion in regard to the early cases reported, it is thought desirable to present them in detail, in table 1.

The first case of sarcoma of the bladder was reported by Senftleben in 1861 and the diagnosis was confirmed by Billroth in 1905. Rabson in 1934 collected 234 cases of sarcoma of the bladder, and since then 48 additional cases have been reported. In a series of 3,435 cases of vesical neoplasm, collected from the works of thirteen authors, Rabson found only 23 cases of sarcoma (0.67 per cent). Pack and LeFevre in their study of 19,129 admissions to the Memorial Hospital found 522 vesical tumors, of which only 3 were not epithelial in origin, namely, 2 sarcomas and 1 leiomyoma, or approximately 1 sarcoma in 10,000 admissions.

The first case of leiomyosarcoma was reported by Gussenbauer from Billroth's clinic in 1875. Since then, 13 or more have been described. From the list of vesical sarcomas containing smooth muscle, 8 definitely were diagnosed by the authors as leiomyosarcoma; the other 6 (all

observed prior to 1904) were called myosarcomas, and in the microscopic description of them all the authors described hyperplasia of smooth muscle cells, although in one or two instances it has been stated that this element by no means predominated. However, we felt that the tissue they described would today be classified as leiomyosarcoma. In table 3 is presented a brief summary of the 14 cases of smooth muscle sarcoma.

The origin of vesical sarcoma is a matter of considerable disagreement. Prentis and Arey suggested three methods of increase of smooth muscle cells in the embryo: (1) formation of new cells from the mesenchyme; (2) transformation of the interstitial cells into muscle fibers, and (3) multiplication of their nuclei by mitoses in the more advanced fetal stage. Thus, smooth muscle tumors may arise in the adult by the unrestrained growth of misplaced persistent mesenchymal cells (Cohen).

The theory has been advanced that myoma is of embryologic origin, developing, according to various authers, from a partially atrophied müllerian body (Verhoogen), from the urachus (Pilliet and Dupuy), from supernumerary ureters (Riegal) or from a hydatid of Morgagni or the lower layer of the utricle (Hegal). Because of the simplicity of these theories of embryonal origin, Heitz-Boyer and Doré and later DeBerne-Lagarde thought that they should be accepted. Blum suggested that myoma develops from hypertrophied vesical musculature, secondary to chronic inflammatory changes. Claisse (cited by Heitz-Boyer and Doré) concluded that uterine fibroid is produced by perivascular inflammation caused by infective agents acting on the walls of the uterine vessels and that the same theory is applicable to vesical tumors. The origin of leiomyoma of the bladder is undoubtedly related to that of leiomyosarcoma.

In writing of leiomyosarcoma Cohen stated that the cells of this tumor are shorter and rounder than those of a benign tumor. The nuclei are massive and hyperchromic. Giant cell forms may exist. The stroma is scanty, and the walls of the blood vessels are defective. According to Evans, the occurrence of many mitotic figures is a reliable sign of malignancy. Proper and Simpson classified malignant leiomyoma into 3 groups and noted that the malignancy increases proportionately through the following groups: (1) those closely resembling leiomyoma; (2) those having short spindle-shaped cells with oval nuclei; and (3) those having great variation in the morphologic character of the cells.

Cecil stated that vesical sarcoma frequently arises from the trigon or the vesical orifice or from near these structures. Rabson concluded that leiomyosarcoma (as contrasted with rhabdomyosarcoma) is more likely to have a primitive origin in the wall of the urinary bladder. A glance at table 3 will bear this out; of the 14 leiomyosarcomas, 13 were definitely stated to have arisen from the vesical wall (in Burlakov's case the origin

TABLE 3.—*Data on Previously Reported Cases of Leiomyosarcoma of the Bladder*

No.	Year	Author	Sex of Patient	Age of Patient	Location of Lesion	Duration of Symptoms	Symptoms	Operation	Result	Autopsy	Metastases?	Author's Diagnosis
1	1875	Gussenbauer	M	12	Posterior wall	10 mo.	Pain; dysuria; frequency	Suprapubic resection	Left hospital 33 days after operation; well	Not stated	Not stated	Myosarcoma
2	1885	Eve	..	..	Right lateral wall	.....	Specimen only	.....	Bilateral hydronephrosis and hydroureters	Yes	Not stated	Myosarcoma
3	1888	Nicolich	M	47	On all walls	2 weeks	Pain; hematuria; frequency; dysuria	No operation	Death 3½ weeks after onset of symptoms; bilateral hydronephrosis and hydroureters	Yes	No	Myosarcoma
4	1895	Klein	M	10	Posterior wall	10 mo.	Pain; hematuria; dysuria	Partial resection of bladder	Healed	Not stated	Not stated	True myosarcoma
5	1904	Lexer	M	59	Right posterior wall	Not stated	Pain; frequency; urgency; abdominal tumor	Partial resection of bladder and pedicle	Healed	Not stated	Not stated	True myosarcoma
6	1904	Röder	M	49	Lateral wall	4 yr.	Left inguinal pain on urination; palpable tumor in left pelvis (per rectum)	Partial resection of bladder wall and urethra	Death 5 days after operation due to peritonitis	Yes	Not stated	True myosarcoma
7	1927	Burlakov	F	54	Bladder	Not stated	Not stated	No operation	Death	Yes	Not stated	Sarcomatous myoma
8	1928	Hager and Hunt	F	53	Posterior wall	10 days	Hematuria (no frequency or pain)	Transperitoneal resection of bladder	Left hospital 24 days after operation; alive and well 4 yr., 2 mo. after operation	Not stated	Not stated	Leiomyosarcoma
9	1929	Carlor and	M	4	Right							

9	1929	Caylor and Walters	M	4	Right superior and anterior lateral walls	8 mo.	Pain; hematuria; frequency and nocturia; dysuria; incontinence	Resection of wall	Recurrence 2 mo. after operation; death 3 mo. after operation	Not stated	Not stated	Leiomyosarcoma
10	1931	Mintz	M	5	Posterior inferior wall	4 mo.	Pain in stomach; hematuria; frequency; dysuria; vomiting	Suprapubic removal of tumor; palliative ureterotomy	Recurrence; death 1 yr. after operation (18 mo. after onset of symptoms)	No	Recurrence at site	Leiomyosarcoma
11	1932	Krauskopf	F	60	Filled bladder and true pelvis anterior wall	2 yr.	Pain; frequency; incontinence; slight loss of weight; increased size of abdomen	Exploratory laparotomy and removal of tumor	Death 36 days after operation due to anuria	No	Not stated	Leiomyosarcoma
12	1932	Powell	M	74	Right lateral wall	5 weeks	Hematuria; loss of weight (no pain, frequency or dysuria)	Resection of lateral wall	Discharged 6 weeks after operation; death 5 mo. after operation	Yes	No; recurrence at site and whole right trigon	Leiomyosarcoma
13	1937	Weyerbacher and Balch	M	4	Left lateral portion	1 week	Pain; hematuria; frequency; retention; straining	Suprapubic cystotomy for drainage; biopsy	Death 3 months after operation	Yes	To lungs	Leiomyosarcoma
14	1937	Kretschmer and Doehring	M	55	Bladder wall	5 yr.	Pain; hematuria; frequency; complete retention; loss of weight; backache; burning	Resection of tumor; fulguration; suprapubic cystotomy; implantation of radium; 55607 mg. hours	Death 1 year after operation	Yes	No	Leiomyosarcoma
15	1937	Ashburn and Wollenweber	M	59	Left side of bladder	Not definite	Pain in bladder; small stream; nocturia; burning; no hematuria	Suprapubic cystostomy	Died	Yes	No metastatic deposits found	Leiomyosarcoma

is not mentioned). Three rhabdomyomas have been reported as arising from the trigon or neck of the bladder (Davoni; MacKenzie and Chase; White).

Age.—The general opinion prevails that sarcoma of the bladder occurs relatively more frequently in the very young (children under the age of 5 years) and in persons past 50. A review of the 14 cases of leiomyosarcoma does not tally with this opinion so far as sarcomas in general are concerned. In our series of 14 cases of sarcoma, the lesions in only 3, or about 20 per cent, occurred in children between the ages of 1 and 5 years, whereas there were 10 patients between the ages of 50 and 60. The age distribution is summarized in table 5.

Sex.—In our series of 14 cases, 10 lesions occurred in males and 3 in females. In 1 case the sex of the patient was not stated.

TABLE 4.—*Location of Lesion*

Position of the Tumor	Number of Cases
Posterior wall	5
Anterior wall	1
Right or left lateral	5
All walls	2
Not stated	1
Total	14

TABLE 5.—*Age Incidence in Cases of Leiomyosarcoma of the Urinary Bladder*

Age	Cases
1- 5 years	3
6-10 years	1
11-20 years	1
21-30 years	0
31-40 years	0
41-50 years	2
51-60 years	4
61-70 years	1
70 years	1
Not stated	1
Total	14

Symptoms.—The symptoms varied within wide limits. In 8 of the 14 cases the presence of hematuria was recorded. On the other hand, there were only 2 cases in which its absence was mentioned. In 10 cases there was pain, and in only 2 cases was pain absent. In one-half the cases the symptoms were of less than ten months' duration. Neither clinically nor grossly can leiomyosarcoma be distinguished from other vesical neoplasms. The diagnosis must be based entirely on the microscopic examination.

It is interesting in this connection to note that the preoperative diagnosis in the case first presented was papillary carcinoma and that the diagnosis was so recorded from the first specimen removed at the time of the first cystoscopic examination. The diagnosis made from a second

specimen removed at the time the suprapubic cystostomy was done was recorded as carcinoma, and it was not until careful study of the autopsy specimen was carried out that the diagnosis of leiomyosarcoma was established.

In this connection it is interesting to note that the cystographic appearance of the bladder was normal.

Metastases.—Metastases were rare with sarcoma as well as with leiomyosarcoma. In our series of 14 cases, metastasis occurred in only 1 instance (to the lungs). Autopsies were performed in 6 cases besides our own, and in none of them was metastasis mentioned, whereas in 3 the definite statement was made that metastasis was not present. Implantation or regional recurrence occurred in 2 instances (Mintz and Powell).

Since in most cases leiomyosarcoma originates from the muscle layer of the bladder and thence invades the wall, wide resection of the bladder must be carried out. In spite of radical removal, however, the outcome, with few exceptions, has been death soon after operation. Only 1 patient was alive and well four years and two months after operation, when last heard from in 1932 (Hager and Hunt).

SUMMARY

A case of leiomyosarcoma of the urinary bladder is described.

A summary of 14 such cases is given, in 8 of which the diagnosis was positive and in 6 of which the tumor was described but was not diagnosed as leiomyosarcoma.

Leiomyosarcoma usually occurs in a patient under the age of 12 years or over the age of 45. In most instances the lesion arises from the wall of the bladder.

Metastasis is rare.

Although the tumor in the case reported was enormous, attention should be called to the fact that the cystographic appearance of the bladder was normal. The correct diagnosis was not made until careful study of the autopsy specimen was carried out.

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SPINAL ANESTHESIA

REGULATION OF HEIGHT WITH FRACTIONAL DOSES

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CINCINNATI

The popularity of spinal anesthesia has undergone various accessions and regressions since its discovery by Corning in 1888. In the hands of such master surgeons as Matas, who was the first in this country to perform an operation employing it, spinal anesthesia proved satisfactory; but for others less experienced and resourceful, it gave unsatisfactory results.

During the second decade of the present century interest in the production of anesthesia by regional injections seems largely to have died out, and the advent of the World War put a temporary embargo on such physiologic experimentation as might have provided better and safer means of administering it. A full decade after the war ended, however, Pitkin brought forward his "controllable" spinal anesthesia, a method which was almost immediately to revolutionize the previous conceptions of the hazards and inconveniences of this particular form of surgical analgesia.

Briefly, the drawbacks had always been (1) a tremendous fall in blood pressure about ten minutes after the administration of the drug employed to induce insensibility and (2) the extremely rapid diffusion of the drug in the spinal canal, which no measure heretofore known had been able to keep under control.

The lowering of blood pressure is, in all probability, due to splanchnic dilatation, which, by causing cerebral anemia, used frequently to prove fatal. Soon after the World War, Labat [1] advocated that the patient be placed in the Trendelenburg position, which was found to reduce the withdrawal of blood from the cerebrum but did not help control the vomiting and retching that intraspinal administration of large doses of anesthetics was almost certain to induce.

Inability to control the extent of the diffusion of the drug in the spinal canal remained an insurmountable obstacle in the way of general

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From the Department of Surgery of the De Courcy Clinic.

1. Labat, G.: Elimination of the Dangers of Spinal Anesthesia, Am. J. Surg. 5:625, 1928.

employment of this form of anesthesia until Pitkin [2] brought forward his method in 1927. In brief, this consisted of employing a solution of lower specific gravity than that of the spinal fluid, having a viscous consistency which makes it less diffusible, and of placing the patient on a table which could be readily tilted to any desired degree, thus making the angle of the patient's body aid in stopping the ascent of the anesthetizing fluid at the required level of insensibility.

The solution which Pitkin recommended, known as spinocain, is made up of 200 mg. of procaine hydrochloride and 2.2 mg. of strychnine sulfate, dissolved in 14.5 per cent alcohol and sterile water, to which an amyloprolamine combination has been added. This product is a viscous fluid of specific gravity so much less than that of the spinal fluid that it floats on the latter "like the air bubble of a spirit level."

An intradermal injection of a solution containing 1 per cent procaine hydrochloride and 5 per cent ephedrine hydrochloride was made at the site of spinal puncture to render the skin insensible, thus facilitating the introduction of the spinal needle and preventing a too rapid fall in blood pressure. The injection was made with the patient on his side on the level table. When injection was completed the table was immediately tilted to the angle needed to permit diffusion of the anesthetic to the upper limit of the portion of the body on which operation was to be done. For example, with the table tilted so that the patient is in the 15 degree Trendelenburg position, anesthesia will be limited to the perineum and the lower extremities; tilting to the 10 degree level permits diffusion as high as the umbilicus; at 5 degrees insensibility will be complete as far as the lowest ribs, which is as high as it is desirable to operate with this form of anesthesia. A meter designed by Pitkin [2] to be attached to the table made it possible for operator and anesthetist to know precisely how far the anesthetic would rise.

This method of "controllable" anesthesia aimed to make the hitherto decidedly uncertain and hazardous spinal method relatively safe and sure in the hands of experienced and careful operators. My associates and I began to employ it in our clinic soon after Pitkin made his first presentations, so that by 1930 it was possible to report a series of five hundred major operations wherein this form of anesthesia had been used.[3] We had made it a routine in appendectomy, cholecystectomy, gastroenterostomy and nephrectomy. We had also employed it widely when carrying out procedures on the uterus, prostate, rectum and

2. Pitkin, G. P.: Controllable Spinal Anesthesia, J. M. Soc. New Jersey **24**: 425, 1927.

3. De Courcy, J. L.: Use of Controllable Spinal Anesthesia in Five Hundred Major Operations, Ohio State M. J. **26**:397, 1930.

perineum, as well as in amputations of the lower limbs. The complete relaxation afforded by spinal anesthesia and the absence of straining were particular advantages offered by this method.[4]

Yet despite the great advance of Pitkin's method over anything previously offered for surgical anesthesia, as time went on we found that a number of serious drawbacks attended it. The theory in regard to the nondissemination of the anesthetizing fluid above the desired level was found in practice to fail occasionally. In other words, the anesthesia was not as "controllable" as we would have liked. Also, the postoperative vomiting and retching could not always be eliminated when the quantities advocated by Pitkin were used.

Three years ago we set about improving the method, our chief aim being to limit the ascent of the anesthetizing fluid in the spinal canal and at the same time to minimize the unpleasant after-effects by reduction of the amount of anesthetizing drug needed to produce insensibility to pain in a given area. We experimented to discover how small a quantity of anesthetic agent we could use while still inducing perfect anesthesia and affording time enough for thorough and painstaking surgical procedures. We abandoned spinocain because of its occasionally unfavorable reactions, and now we make use of procaine hydrochloride exclusively, because we have found it less toxic and more uniform in its action.

With the doses which will be mentioned shortly we have had a high degree of satisfaction. The formerly dreaded fall in blood pressure has been absent, while retching and vomiting, which so often impeded us and distressed our patients, have been practically abolished. In a series of 100 cases in which spinal anesthesia was used for operations of various types, vomiting took place but six times. All the operations were on the lower part of the abdomen, for we have found it expedient not to employ general anesthesia for intervention above the umbilicus.[5]

Though this work was aimed primarily at reduction of the dose, the most important thing demonstrated has been the impossibility of abiding by any hard and fast rule. Irrespective of the height which the anesthetizing fluid is required to attain, the same dose should not be used in every case. Fractional dosage, with as little of the anesthetic agent as possible, is of the greatest aid in lessening and eliminating the distressing sequelae once so often witnessed after employment of the earlier methods of applying spinal anesthesia.

Whereas formerly we gave up to 200 mg. in order to perform a prostatectomy or an appendectomy and all too often saw the disagreeable

4. De Courcy, J. L.: Newer Methods of Controllable Spinal Anesthesia: Use of Pitkin's Method in One Hundred Cases, Am. J. Surg. **5**:620, 1928.

5. De Courcy, J. L.: Acute Intestinal Obstruction, Am. J. Surg. **35**:532, 1937.

results of which mention has just been made, we are now performing these same operations satisfactorily when using hardly more than a quarter of the amount of drug once thought necessary. We find that 50 mg. of procaine hydrochloride, mixed with 1 cc. of spinal fluid (barbotized), is sufficient to produce an insensibility which will permit intervention on any tissues located below the course of an imaginary line drawn between the two anteroposterior spines of the ilium. This class of intervention includes suprapubic prostatectomy, replacement of uterine prolapse (if done by the vaginal route), intervention for inguinal hernia and amputation or other operation on the legs. Hemorrhoids can be painlessly removed when no more than 25 mg. of procaine hydrochloride has been injected, and 100 mg. will induce perfect anesthesia for an hour, which is ample time to permit the removal of stones from the kidney and renal pelvis, or complete nephrectomy, as well as cholecystectomy or adrenalectomy.[6] With as little as 75 mg. the anesthesia can be raised above the umbilicus, almost as high as the ensiform cartilage, which allows the performance of such operations as appendectomy and abdominal hysterectomy.

These quantities, it will be observed, are much less than those now being recommended as a routine for spinal anesthesia. For example, King,[7] writing in February 1935, said that workers in his clinic (Pennsylvania Hospital, Philadelphia) dissolve procaine hydrochloride crystals directly in the withdrawn spinal fluid, using 1 cc. of fluid with from 0.05 to 0.10 Gm. of the drug injected in the fourth lumbar space, to produce half hour anesthesia of the perineum, the prostatic bed and the pelvic organs, and (using the greatest amount) one hour anesthesia of the upper pelvic and lower abdominal structures. To this, 50 mg. of ephedrine is routinely added.

In a recently published article, on spinal anesthesia, with special reference to dosage, Atwood [8] reviewed the amounts of anesthetic drugs now in use for spinal injection in different parts of the country. This writer himself, at the advice of William Ross Jr., employs 50 mg. of procaine hydrochloride in a "small amount of spinal fluid" as a routine for urologic procedures lasting from one to one and a half hours. For general surgical work he uses "not over 120 mg. of novocain [procaine] dissolved in two measured cc. of spinal fluid," which gives "a concentration up to 6.16 per cent on injected fluid."

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6. De Courcy, J. L.: Technique of Adrenalectomy and Adrenal Denervation, Am. J. Surg. **30**:404, 1935.

7. King, O. C.: Spinal Analgesia: Report of Fifteen Hundred Cases, Ann. Surg. **101**:690, 1935.

8. Atwood, H. S.: Spinal Anesthesia, with Special Reference to Dosage, Northwest Med. **36**:350, 1937.

At the Mayo Clinic concentrations of between 3 and 5 per cent are used, as there procaine hydrochloride is not considered destructive if the concentration is no more than 17 per cent. For appendectomy, Atwood has had satisfactory anesthesia with 60, 70 and 80 mg., but when only 50 mg. was injected the patient experienced severe pain, so that now 100 to 120 mg. is usually employed.

As the perineum is served by nerves from the lowest part of the spinal canal, it follows that the least volume of anesthetic drug will be required to make it insensible. Evans [9] in 1936 reported carrying out in this region operative procedures which caused the patient no pain whatever when only 25 mg. of procaine hydrochloride had been injected. This is a smaller amount than that which we have required for the production of anesthesia of the tissues, even in the perineal region. But for work higher up this same operator used 150 mg. in 2.5 cc. of spinal fluid, and for what may be termed a "high spinal injection" he employed 14 cc. of a 1:1,500 solution of procaine hydrochloride.

These citations will serve to demonstrate that the tendency among the majority of operators now is away from large dosage, but I feel that sufficient emphasis has not as yet been laid on the importance of this reduction. During the three years since a consistent effort has been made in our clinic to follow the conservative course which I outlined earlier in this article, there has been a steady improvement not only in the results in our operating room but in the postoperative course of our patients as well, and in the remote results of the operation in cases followed for a long period after operative recovery. We have likewise been able to use spinal anesthesia on patients for whom this would have been absolutely contraindicated at the time when we were employing larger doses and have used it in procedures wherein previously we would not have considered it safe.

As an example the relief of acute intestinal obstruction may be cited. Inhalation methods are not indicated in cases of such obstruction because there is so much danger involved in vomiting or in the aspiration of the gastric content by the unconscious patient. Often such a case does not come under observation until the patient has become profoundly toxic. To a person in this state administration of gas or ether may well prove highly dangerous or even fatal. As I advocated in a previous paper,[5] for these patients it is best to employ 100 mg. of procaine hydrochloride, which is sufficient for a long exploratory incision, or 75 mg. if the site of the procedure is low, as for cecostomy. For some years now I have advocated spinal methods, with careful sedative medication both before and after the actual procedure, for operations of the type of adrenalectomy, which has been satisfactorily performed with 100 mg. of procaine

9. Evans, F.: Anesthesia in Rectal Surgery, Post-Grad. M. J. **12**:345, 1936.

hydrochloride, diluted with 1 cc. of spinal fluid, barbotized only twice. With this small dose vomiting rarely occurs, and the anesthesia remains perfect for almost an hour, ample time for performance of a painstaking operation. The medication consists of ¼ grain (0.0162 Gm.) of morphine sulfate and 1/150 grain (0.0004 Gm.) of scopolamine hydrobromide, given three quarters of an hour before operation. An additional safeguard is the administration of ephedrine immediately after injection of the anesthetic and as often while the operation is in progress as the state of the pulse and of the blood pressure would seem to indicate.[6] It is always given intramuscularly. As a routine we allow ten minutes to elapse after injection of the anesthetic before making any attempt to start the surgical incision, the anesthetist meanwhile from time to time making the customary tests for sensibility.

Since adoption of the fractional dose method we have had no fatalities among cases of surgical intervention which could in any way be attributed directly to the effects of the anesthetic. To be sure, we select the subjects for spinal injection with considerable care. We never use the method when the patient is a distinctly "bad risk," even if he presents conditions which strongly contraindicate any form of inhalation technic. In general, we avoid the spinal method in any type of high abdominal work, although I have mentioned that we sometimes use it in cases of acute obstruction of the intestine, when the point of blocking is far down in the canal.

Whether a surgeon should use spinal anesthesia for certain abdominal operations is a matter of personal preference. We have found it better to employ inhalation methods for resection of the stomach and other procedures of that general type, although the administration of 150 mg. of procaine hydrochloride is regularly sufficient to raise the area of insensibility as high up as the nipple line, thus permitting intervention on any structure below the diaphragm. In regard to this Atwood[8] said: "The higher the spinal the more danger of embarrassment of respiration and the more vital becomes the administration of small doses." This strikingly confirms our own experience.

No matter how much confidence the operator has in his ability to control the dose when administering an anesthetic spinally, if he is wise he will not fail to have on hand everything he may need should an emergency arise. A suitable blood donor should always be on call, and the facilities for a transfusion either of blood or of acacia or dextrose should be kept within easy reach. If there is any unavoidable delay, if a traumatic accident occurs or if for any reason, hemorrhage is unduly profuse, such precautions may save not only the patient's life but the operator's reputation, and they may prevent the method of anesthesia from being blamed for results for which it was in no way responsible.

While this method is now called "controllable" anesthesia, it is necessary not to lose sight of the fact that the greater safety of inhalation methods resides largely in the ease with which the anesthetic can be entirely withdrawn as soon as an ill effect on the patient is observed. No injected anesthetic enjoys this advantage. North [10] has truly said, "The great peril of spinal anesthesia lies in the uncontrollable nature of its accidents." The same, of course, is true of rectal and intravenous anesthesia.

For operations which may be done in bed or for relatively simple procedures such as those for hernia or recurrent appendicitis, the spinal method is ideal, since in this type of intervention the patient's general state remains practically the same throughout. In more extensive operations, however, wherein great trauma to the tissues, loss of blood and a general lowering of physical tonus are involved even if an actual state of shock does not supervene, the inflexibility of the spinal method is a grave drawback, for the patient's physical tone is rapidly lowered by hemorrhage and shock, while the amount of anesthetic drug injected remains the same. Consequently, the actual dose to the depleted patient is much higher than it should be, yet one is powerless to withdraw it as one would an inhaled anesthetic. With the inhalation method, one can do even more: by washing out ether or nitrous oxide with oxygen, the anesthetic agent can be removed immediately. This gives the inhalation method a vast advantage over injection of any form of drug.

Against these increased dangers should be set spinal anesthesia's undoubted advantages, chief among which—from the surgeon's point of view—is the complete relaxation it affords. This is of such great aid in operation on the intestinal tract that one is tempted to use the method for those abdominal procedures where perfect relaxation is highly essential to satisfactory work. With sufficient experience and technical skill, spinal or intravenous anesthesia or rectal administration of avertin with amylene hydrate may be employed in abdominal work, even above the umbilicus; yet it must never for a moment be forgotten that these methods of anesthesia are inflexible and that the utmost caution must at all times be employed in their use, especially if the patient has been classed as a "bad risk."

While it is impossible altogether to do away with these inherent dangers, they can be minimized considerably. This, I believe, the method of fractional dosage has done much to accomplish. I am convinced that a systematic use of as little of the anesthetic agent as possible will not only increase the safety of the method but will help abolish the unpleasant after-effects, such as headache, nausea and vomiting, and will

10. North, J. P.: Use and Abuse of Spinal Anesthesia, Ann. Surg. **101**:702, 1935.

give a smoother, more comfortable convalescence than is the lot of the patient operated on under inhalation anesthesia. Both surgeons and specializing anesthetists should labor to perfect themselves in the technic of administration.

Most careful physical examination should be given to every candidate for this type of anesthesia, and the results should be interpreted in terms of the diathesis of the person under consideration. It is not enough to segregate persons with evident abnormalities, such as diabetes or advanced renal impairment. Most of the deaths directly attributable to spinal anesthesia have occurred because some contraindicating factor was overlooked at the preoperative physical examination. The responsibility placed on the surgeon is a great one.

The "safer" anesthetics are also the "easier" ones. Nevertheless, the ever widening employment of spinal anesthesia and the increased demand for it by patients about to undergo operation show that the method is already established in a position of favor from which it would be difficult indeed to dislodge it. Constant care and study for improvement are the only alternative.

CONCLUSIONS

1. Fractional dosage in spinal anesthesia, with as small a dose as is capable of inducing insensibility in the tissues to be operated on, greatly increases the safety and extends the applicability of the method.

2. The height to which the anesthetizing drug rises depends on the dose employed and, to a lesser degree, on the amount of spinal fluid used to dilute it.

3. We have found procaine hydrochloride the most suitable anesthetic agent, with 1 cc. of spinal fluid used to dilute it irrespective of the amount of the drug.

4. In all cases, irrespective of dose or dilution, the effect of the anesthetic will always last for at least an hour. Duration is not affected by the amount of drug administered.

5. "Bad risk" patients should not be subjected to spinal anesthesia; but, other things being equal, hypotension should not be taken as an absolute contraindication to use of the method. If hemorrhage has occurred, however, or if unusual difficulty is anticipated, inhalation methods are safer.

6. When there are no contraindications, spinal anesthesia is used in our clinic for any operation to be performed below the umbilicus.

FRACTURES OF THE UPPER EXTREMITY AND THE SHAFT OF THE HUMERUS

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The purpose of this presentation is to review and evaluate the results obtained in treatment of fractures of the upper extremity and shaft of the humerus by the use of traction with the arm in abduction.[1] Since that treatment has been applied as a matter of routine in the majority of cases, an excellent opportunity is afforded for defining the uses and limitations of the traction-abduction treatment for fractures of the arm. The series includes all the cases in which such fractures were treated in the Beekman Street Hospital, New York, by the various members of the staff from 1929 to 1934 inclusive.

There were 106 fractures of the upper extremity and shaft of the humerus: 17 fractures of the greater tuberosity, 46 fractures of the surgical neck and 43 fractures of the shaft. Fractures of the shaft included 11 fractures of the upper third, 23 fractures of the middle third and 9 fractures of the lower third. Sixty-three, or over 60 per cent, of the 106 fractures involved the head or the surgical neck.

There were 5 deaths, 4 of which were caused by associated injuries in which the humeral fracture played a minor part. The fifth was exceptional and is discussed under the subject of fractures of the greater tuberosity. Amputation was necessitated in 2 instances because of associated injuries. Eight patients were discharged during the course of treatment, against advice or by request.

Two cases of nonunion appear in this compilation. The patients in both were originally treated elsewhere and were operated on for the preexisting nonunion. Exclusive of the cases of nonunion, in 7 cases open reductions were performed and in 1 permission was refused, making a total of 8 cases in which operation was deemed advisable. Judging from the results, 1 other might be added, making a total of 9, or 8.4 per cent. All of the open reductions were performed because of persistent malposition, and it is probable that the fractures in some cases would have failed to unite without open reduction.

In accordance with general experience, the proximity of the fracture to the shoulder joint varied directly with the age of the patient.

The percentage of fractures requiring open reduction in any series will depend on two factors, the proficiency of the surgeon in perform-

1. Blake, J. A., and Bulkley, K.: The Treatment of Fractures of the Extremities by Means of Suspension and Traction, Surg., Gynec. & Obst. **26**:245 (March) 1918.

ing closed reduction and the degree of anatomic reduction regarded as adequate. In this connection it is interesting to note that all displacements of the neck and upper third of the shaft which were treated by open reduction, with 1 exception, can be duplicated by cases in which the fracture was successfully reduced by closed reduction. The exception was a lateral displacement of the distal fragment in fracture of the upper

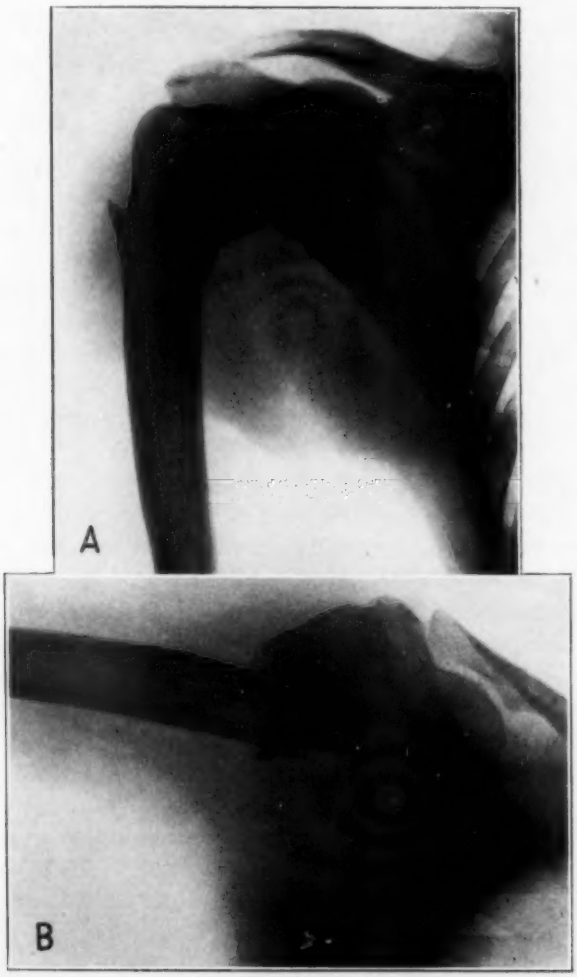

Fig. 1 (case 77).—*A*, fracture of the surgical neck of the humerus. The roentgenogram was taken on the patient's admission to the clinic, with the arm in adduction (anteroposterior view). Note the angulation; the apex of the angle is lateral. *B*, arm in abduction. Note the reversal of the angulation.

third of the shaft, of which there were 2 examples. It is also noteworthy that the fractures were transverse in 8 of the 9 cases in which open reduction was done, in the case in which the patient refused opera-

tion and in both cases in which the patients were admitted for nonunion. This corresponds with the well recognized fact that traction is least effective for transverse fracture and that such a fracture is the fracture which most frequently results in nonunion. A few years ago it was felt that because of the small number of open reductions performed in this clinic the opportunity did not permit any one surgeon to acquire proficiency in operative measures, and since then all such operations have been assigned to one member of the staff. The improvement in operative results has amply justified this change in regimen.

Thirty-three, or approximately one third, of the fractures were the result of traffic injuries. Twenty-four patients suffered severe associated injuries. As has been mentioned, associated injuries resulted in 4 deaths.

There were 3 pathologic fractures, all of which healed without incident. No fracture in this series resulted from a neoplasm.

Callus was noted roentgenologically at four weeks and clinical union at between five and six weeks on the average. It has been the rule to hospitalize patients who are being treated by traction until clinical union has occurred.

It is to be noted that fracture of the greater tuberosity was more than twice as frequent on the right side, whereas the incidence of other fractures was nearly reversed. This inconsistency might be explained by the fact that the former usually resulted from indirect injury and the latter more often from direct violence. In indirect trauma the more efficient arm is instinctively used to ward off injury, and the less expert arm is more vulnerable to direct trauma.

Seven patients had compound fractures, and all the fractures occurred in the shaft. For only 1 of these was débridement done, and amputation was later required because of associated injuries (thrombosis of the axillary artery and tear of the brachial plexus). Infection played no part in the results, all the fractures healing without infection. The number of compound fractures does not warrant a discussion of their treatment. I should like to call attention, however, to the fact that this series presents no evidence for justification of the more radical active treatment of compound fracture which at present seems to be gaining ascendancy. I believe that compound fracture of the lower extremities should be treated more radically than compound fracture of the upper extremities because of the increased danger of infection.

Incomplete palsy of the radial nerve was noted in a few instances. Operative relief was required in only 2 cases; the patient in 1 was admitted for nonunion. Open reduction was indicated in both, irrespective of the involvement of the nerve. Permanent impairment of the radial nerve did not occur in any case in this series.

The impression is widespread that disability of the shoulder joint is more marked than disability caused by similar fractures of the hip joint.

I believe that this relative discrepancy is more apparent than real. The range of motion of the upper extremity is so much greater that a proportionate loss of motion is more apparent. Loss of function of the shoulder is more noticeable to the patient because the extreme range of motion at the shoulder is employed more frequently by elderly persons than is that of the hip. Except in fractures of the head and surgical neck, motion at the scapulohumeral joint is commonly regained completely. One fracture of the surgical neck and head showed complete

Fig. 2 (case 10).—Fracture of the surgical neck of the humerus, lateral view. There is angulation, with the apex of the angle anterior. The coracoid process is seen projected forward to the right; the acromion process can be seen superimposed on the head.

loss of function of the scapulohumeral joint. This case is discussed in the present paper.

The Blum adaptation of Russell traction has been used in 8 cases of this series. My experience with this method is not sufficiently extensive to justify extended comment.[2] However, in addition to permitting

2. Blum, L.: Double Pulley Traction in Fractures of the Shaft of the Humerus, J. A. M. A. **101**:1953 (Dec. 16) 1933.

abduction and external rotation, it allows the application of considerably more traction, since the entire forearm and wrist gives a more effective surface for pull than does the upper part of the arm, with the addition of the accessory pull at the elbow joint. If still more traction is desired, a Kirschner wire may be inserted through the lower end of the humerus or the olecranon and skeletal traction applied directly to the humerus. Skeletal traction was employed only twice in this series.

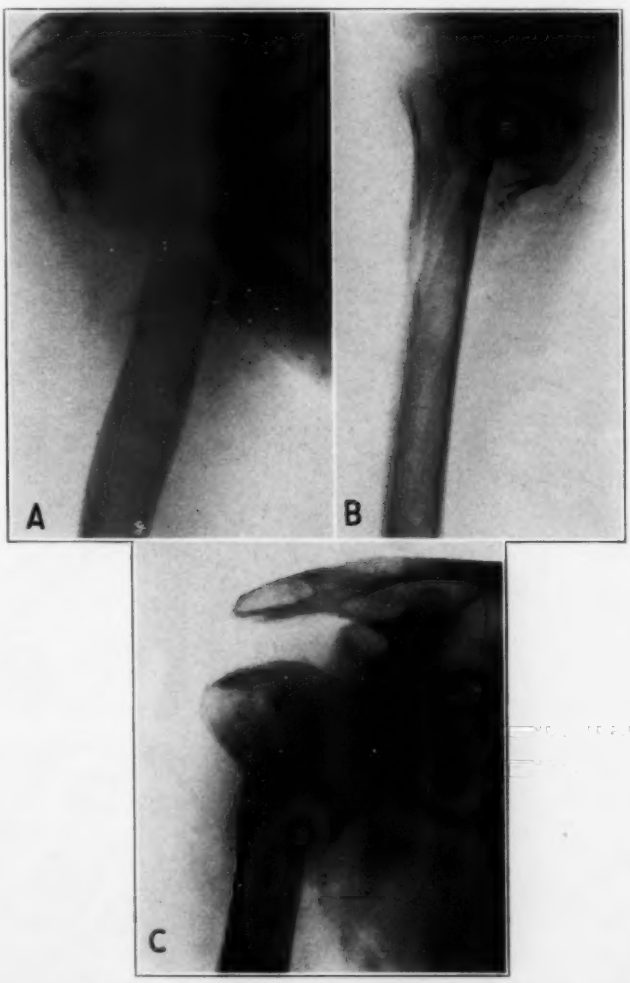

Fig. 3.—*A*, fracture of the surgical neck and head of the humerus, with complete medial displacement and overriding. The roentgenogram was taken on the patient's admission to the hospital. *B*, same fracture four weeks after reduction (lateral view). There is anterior displacement of the shaft of about 50 per cent. *C*, same fracture eight weeks after reduction (anteroposterior view). Callus is evident.

Fracture of the Greater Tuberosity.—There were 17 fractures of the greater tuberosity alone, 12 occurring as complications of dislocations

TABLE 1.—*Fractures of the Greater Tuberosity*

Number	Age of Patient	Sex of Patient	Arm	Compound or Simple Fractures	Dislocation	Treatment	Duration of Traction	Duration of Hospitalization	Associated Injuries Other Than Dislocations	Follow-Up	Result		Comment
											Anatomic	Functional	
11	49	M	R	S	D	Closed reduction; traction 6-8 lb. (2.7-3.6 Kg.)	14	14	0	0	4	4	Result at discharge
12	44	M	R	S	D	Closed reduction; immobilization	..	5	0	0	..	..	
13	30	F	R	S	D	Closed reduction; immobilization	..	3	0	0	..	..	Left against advice
14	64	M	R	S	0	Sling; active motion	..	16	0	0	..	..	Remained for diabetic treatment
31	48	M	L	S	D	Closed reduction; immobilization	..	16	Cerebral concussion	0	..	..	
34	50	M	R	S	0	Sling; active motion	..	20	0	5 yr.	4	3	Repair of hernia
35	72	F	R	S	0	Sling; active motion	..	15	Cerebral concussion	4 mo.	4	3	
36	45	F	R	S	D	Closed reduction; traction 3-4 lb. (1.3-1.8 Kg.)	26	31	0	0	..	..	
37	57	M	R	S	D	Closed reduction; traction	17	20	0		Died		Hematogenous infection of shoulder (B. mucosus capsulatus)
57	58	F	L	S	D	Closed reduction; immobilization	..	2	0	0	..	..	
59	54	F	R	S	D	Closed reduction; traction	10	20	0	1½ yr.	4	4	Hypertension; obesity
70	46	M	L	S	D	Closed reduction; traction	13	19	0	6 mo.	4	3	
80	61	M	R	S	D	Closed reduction	..	8	0	0	..	..	Hypertension; chronic nephritis; chronic otitis media; arteriosclerosis; bilateral hernia
88	39	M	L	S	D	Closed reduction; traction of 10 lb. (4.5 Kg.)	25	31	0	1½ yr.	4	4	Fracture of surgical neck of same arm 8 weeks later
89	44	M	L	S	0	Traction	23	23	Burn of arm and hand	0	..	..	
91	26	M	R	S	D	Closed reduction; traction	9	11	0	0	..	..	
93	49	M	R	S	0	Sling; active motion	..	32	Fracture of tibia and shaft of fibula	0	..	..	

of the head of the humerus. Displacement in every case in which it occurred was associated with dislocation, and reduction of the dislocation resulted in satisfactory reduction of the displacement. In no case was open reduction indicated. A fracture of this type should be looked for in all cases of dislocation of the humerus.

There was 1 death in this group, the only death in the entire series in which the humeral injury was an important factor. The patient was a man aged 57, who had been suffering from enteritis for several years. He had fallen on his right shoulder two days before admission. On admission he had a subcoracoid dislocation and a fracture of the greater tuberosity, with marked displacement. A closed reduction was performed with the patient under ether anesthesia. He was suffering from

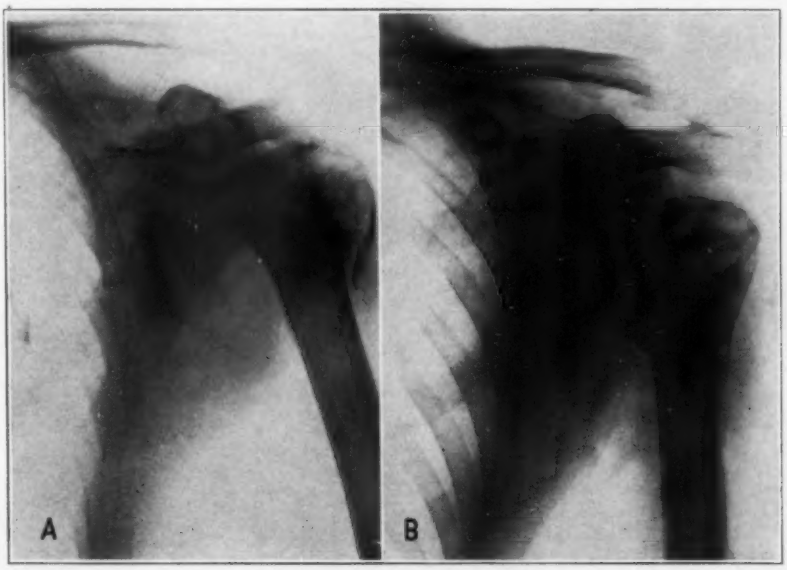

Fig. 4 (case 2).—*A*, fracture of the surgical neck and head of the humerus and subcoracoid dislocation of the shoulder after reduction. Note the portion of the head which has remained in a subcoracoid position. *B*, same fracture after four months. Note the reformation of the neck to the subcoracoid portion of the head.

diarrhea and had a septic temperature, with leukocytosis. Thirteen days after his admission to the hospital, fluid was found in the shoulder joint and was aspirated. The following day through and through drainage of the joint was instituted, and the patient died five days later of sepsis. Cultures of the fluid showed Bacillus mucosus capsulatus. Cultures of the blood were consistently sterile. It is surprising that such experiences are so rare. If open operation had been performed, the surgeon would have borne the onus of infection and death.

The follow-up results, obtained in only 35 per cent of cases, are too incomplete for satisfactory analysis. However, 2 A4-F4 results and 1

TABLE 2.—*Fractures of the Surgical Neck of the Humerus*

Number	Age of Patient	Sex of Patient	Arm	Simple or Compound Fracture	Treatment	Duration of Traction	Duration of Hospitalization	Associated Injuries	Follow-Up	Result: Anatomic	Result: Functional	Comment
1	68	F	L	S	Blake traction, 6-8 lb. (2.7-3.6 Kg.)	45	58	0	4½ mo.	4	3	Abduction 90°
2	69	M	L	S	Closed reduction	..	1	Dislocation of shoulder	5 mo.	2	2	No motion in scapulohumeral joint
5	64	M	R	S	Blake traction, 6-7 lb. (2.7-3.2 Kg.)	38	50	0	9 mo.	4	3	Abduction 135; internal rotation 45; external rotation 45
6	56	F	L	S	Blake traction 6 lb. (2.7 Kg.)	28	32	0	1 yr.	4	4	Colle's fracture 2 mo. before (left)
8	42	F	L	S	Blake traction 4-6 lb. (1.8-2.7 Kg.)	35	42	0	.....	4	3	Abduction 170; slight limitation internal rotation
10	49	M	L	S	Closed reduction; operation; traction	17	51	0	6 mo.	4	3	Open reduction 18th day; abduction 150°, rotation complete
15	65	M	L	S	Blake traction 5-6 lb. (2.3-2.7 Kg.)	39	43	0	10 mo.	4	4	
16	48	F	L	S	Blake traction 6 lb.; Kirschner wire; closed reduction	..	..	0	.....	..	..	
17	58	M	L	S	Closed reduction; Blake traction 6 lb. (2.7 Kg.)	4	5	0	.....	..	..	Plaster spica in abduction; left against advice
18	51	M	L	S	Blake traction 10 lb. (4.5 Kg.)	5	5	0	0	..	..	Transferred; alcoholism
19	65	M	L	S	.....	..	..	.....	.....	..	..	Transferred day of admission
20	32	M	R	S	Blake traction 6-8 lb. (2.7-3.6 Kg.)	41	43	0	0	4	3	At discharge
21	68	M	L	S	Blake traction 8 lb. (3.6 Kg.)	15	16	0	0	..	..	Left against advice; airplane splint
22	26	F	L	S	Blake traction 3 lb. (1.3 Kg.)	12	13	Concussion fr. nose	4 yr.	4	4	
23	65	M	L	S	Active motion	..	44	Fracture of left clavicle, right fibula, middle phalanx left 5th finger	7 mo.	4	3	Fell 10 feet; shock; diabetes
			R	S	Active motion					4	2	
25	15	M	L	S	Blake traction	17	21	0	4 mo.	4	4	
26	65	M	R	S	Active motion	..	4	0	4 mo.	4	3	
27	34	M	R	S	Blake traction	19	27	0	0	..	..	Epileptic
28	41	F	L	S	Blake traction 5-10 lb. (2.3-4.5 Kg.)	43	50	0	3 mo.	4	3	Arthritis of knees; treatment in clinic prevented
29	62	M	L	S	Blake traction 5-7 lb. (2.3-3.2 Kg.)	27	29	0	5 yr.	4	4	
30	65	M	L	S	Blake traction 6-8 lb. (2.7-3.6 Kg.)	35	38	0	0	..	..	Motion of shoulder excellent on discharge
33	56	M	L	S	Blake traction 5 lb. (2.3 Kg.)	28	32	0	3 mo.	4	4	
39	67	F	R	S	Blake traction	(9)	34	Fracture of external				

33	56	M	L	S	Blake traction 5 lb. (2.3 Kg.)	28	32	0				
39	67	F	R	S	Blake traction	60	84	Fracture of external condyle (right); head of radius (right); dislocation of elbow (right)	.....	..	..	Treatment of elbow complicated by difficulty with retention; signed release
62	11	M	R	S	Closed reduction; Blake traction 5-10 lb. (2.3-4.5 Kg.); open reduction	6	58	0	6 mo.	4	4	Lateral displacement and angulation; nail
67	40	F	R	S	Closed reduction; Blake traction 5-10 lb. (2.3-4.5 Kg.); open reduction	20	72	0	1 yr.	4	4	Lateral displacement and angulation; nail
68	18	M	L	S	Sling; active motion	..	99	Fracture of 11th and 12th left ribs, left clavicle, Colles left; pelvis; hemothorax left; contusion left kidney	0	..	..	Slight limitation of abduction and external rotation at discharge; sailor; fell 40 feet in hold of ship
69	57	M	L	S	Blake traction 8 lb. (3.6 Kg.)	..	..	Fracture of skull; concussion	0	..	..	
73	41	F	R	S	Closed reduction; Blake traction 11 lb. (5 Kg.)	40	44	Fracture of right ulna; dislocation of right radius	5 mo.	4	4	Closed reduction of forearm
74	41	M	L	S	Closed reduction; Blake traction	46	50	0	5 mo.	4	3	Uncooperative
75	13	M	L	S	Blake traction 5-7 lb. (2.3-3.2 Kg.)	28	28	0	5 mo.	4	4	Epiphysial separation
76	49	M	L	S	Blake traction 5 lb. (2.3 Kg.)	19	37	0	1 yr.	4	4	Bilateral hernia repair
77	37	M	R	S	Blake traction 6-10 lb. (2.7-4.5 Kg.)	28	30	0	10 mo.	4	3	Limited rotation
78	17	M	R	S	Blake traction 10 lb. (4.5 Kg.)	18	23	0	1 yr.	4	4	
80	66	M	R	S	Sling; active motion	..	31	0	0	..	..	Syphilis of central nervous system, cord, bladder
84	38	F	L	S	Blake traction 15 lb. (7.3 Kg.)	30	34	0	0	..	..	Abduction complete on discharge
85	55	M	R	S	Blake traction 5-10 lb. (2.3-4.5 Kg.)	32	36	0	4 mo.	4	4	
90	44	M	L	S	Blake traction 15 lb. (7.3 Kg.)	37	39	0	0	..	..	Fracture of greater tuberosity of same arm 2 mo. before
92	28	M	L	S	Blake traction 5-10 lb. (2.3-4.5 Kg.)	31	39	0	3 mo.	4	4	
96	49	M	L	S	Closed reduction; traction (Blum) 5 lb. (2.3 Kg.)	5	18	0	3 mo.	4	3	Uncooperative; anxiety neurosis
97	73	M	L	S	Blake traction 8-12 lb. (3.6-5.4 Kg.)	20	20	0	0	..	..	Old fracture of skull; senile; complete displacement; refused operation A.O.R.
99	57	M	L	S	Blum traction 6 lb. (2.7 Kg.)	39	40	0	0	..	..	
100	35	M	L	S	Blake traction 7-10 lb. (3.2-4.5 Kg.)	26	39	0	0	..	..	
101	64	M	R	S	Sling; active motion	..	7	0	0	..	..	Injury 3 weeks old
102	67	F	L	S	Sling; active motion	..	6	0	1 yr.	4	3	90 abduction; other motions complete
104	21	F	L	S	Blum traction 3½ lb. (1.5 Kg.)	44	49	0	9 mo.	4	4	Radial paresis; temporary

A4-F3 result, as well as one A4-F4 on discharge were obtained by use of the Blake board with the arm in abduction from ten to twenty-five days. The other 2 patients who showed A4-F3 results were treated with sling and active motion, and the fractures were not complicated by dislocation. These results seem to favor abduction treatment.

Hospitalization varied from two to thirty-two days, with an average of approximately seventeen days. The longer periods were required because of associated injuries or other conditions. In addition to dislocations there were 2 cerebral concussions, 1 fracture of the tibia and the fibula (upper third) and a severe rope burn of the hand and arm in an eighteen story slide. One patient remained for a hernia operation, 1 for diabetic treatment and 1 on account of the hematogenous infection mentioned. One patient suffered a fracture of the surgical neck of the humerus of the same arm while still under treatment in the clinic.

There were no compound fractures in this group.

Fracture of the Surgical Neck.—According to Stimson's classification, only 1 of these fractures was a true fracture of the anatomic neck of the humerus and that was an epiphysial separation of the upper humeral epiphysis, the only epiphysial separation in this series. On the other hand, many of the fractures involved the anatomic neck through most of its extent. Of the 46 so-called fractures of the surgical neck, 14 also involved the greater tuberosity or the head of the humerus, or both. One fracture was bilateral. Only 1 was complicated by dislocation of the head of the humerus.

The ages of the patients varied from 11 to 73 years. The average was 52½. On the whole, therefore, the patients formed an unfavorable age group for function and union.

In the 17 recorded cases callus was present after from seventeen to thirty-eight days, an average of twenty-seven days. Union occurred in from twenty-one to seventy-two days, an average of thirty-seven days. Union was obtained in all cases.

There were no pathologic fractures in this group. Eight patients had severe associated injuries. There were no deaths.

There were no compound fractures. Fractures involving the humeral head and neck are unlikely to be compounded because of the surrounding muscles and tendons.

Fractures of the surgical neck frequently appear impacted on roentgen examination. Firm impaction is the exception and should not be considered when gross displacement is present. Lateral as well as anteroposterior roentgenograms are essential in determining impaction and displacement, a determination which may be difficult because of the obliquity of the fracture line and rotation of the head. There is no typical displacement of either fragment and the weight of the extremity or the fracturing force is the most important factor in causing displacement. For example, on admission there is generally angulation with the

apex of the angle lateral, and after abduction, even though gradual, the angulation is commonly reversed, the apex of the angle being medial. This is true of most of the cases in this series in which roentgenographic diagnoses of impaction had been made. Angulation with the apex anterior is common and usually is not influenced by abduction or traction. In cases with overriding and complete displacement the fracture may be reduced by closed reduction or by skeletal traction. Cutaneous traction alone is not effective in reducing overriding in fractures of the

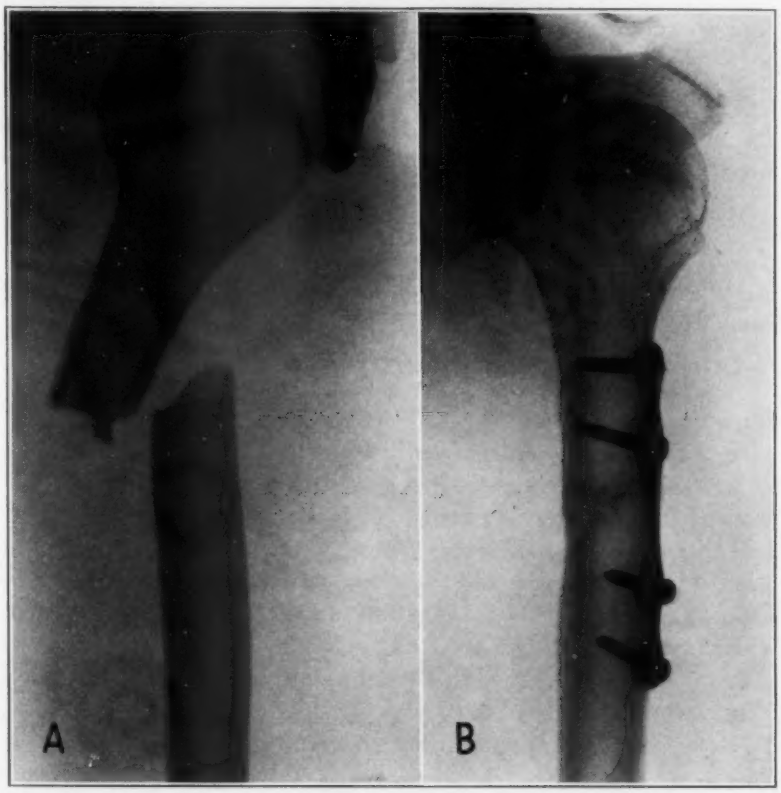

Fig. 5 (case 98).—*A*, fracture of the shaft of the humerus (upper third) with complete lateral displacement and overriding. There were no instances of successful closed reduction of displacements of this type. *B*, same fracture six months after open reduction.

surgical neck. Open reduction was done for 3 patients and refused by 1.

In 1 case (case 2) the injury was complicated by a dislocation and fracture of the humeral head. After reduction a portion of the head remained subcoracoid. This reunited to the shaft and prevented motion at the shoulder joint. It was recognized that this fragment should be removed or reduced, but because of the patient's age (69) and poor general condition no operation was performed. This was the only known

case in which the functional result was poor. It was the only instance of a fracture of the humeral neck complicated by dislocation. Osseous deformities were common roentgenographically, but clinically they were not evident, nor were they known to be responsible for functional disability in any of these cases, other than that aforementioned.

The patient in 1 case (case 97), with a transverse fracture and complete medial and anterior displacement with overriding which was not improved by traction and closed reduction, refused operation. Without operation nonunion was anticipated, but no follow-up was obtained.

Three fractures were treated by open reduction. Two were displaced laterally and anteriorly with the angulation apex medial and were maintained by a nail. The position of one of these (the patient was a child) was not improved. Both had A4-F4 results (cases 62 and 67). In the third case exploration was done on the eighteenth day and showed beginning union and fair position. The fracture was not influenced by the operation. This case was followed for six months and showed an A4-F4 result.

Fracture of the Upper Third of the Shaft.—There were 11 cases of fracture of the upper third of the shaft. The youngest patient was 11 years of age, the oldest 72. The average age was 42. There were 9 male and 2 female patients. Three fractures were compound and the others simple.

One was reduced and treated in plaster. Five were treated by traction, 1 with the Blum apparatus and the rest with Blake board. Two were treated by open operation with the Sherman plate.

In 1 case of compound fracture débridement was done and amputation was later performed because of thrombosis of the axillary artery, beginning gangrene and a tear of the brachial plexus. There were 2 additional compound fractures, both caused by gunshot wounds, which were treated conservatively and which healed without incident.

There were 2 deaths. Both patients died in less than twenty-four hours, of severe associated injuries, never recovering from the initial shock.

One fracture was pathologic; it was caused by a solitary bone cyst occurring in a child of 11. The cyst had largely disappeared three months after the fracture.

In 1 case there was delayed union (fifty-four days) as a result of poor apposition, treated by Blake traction. Open operation was seriously considered in this case but was deferred as crepitus was easily elicited. A follow-up after twenty months showed an A4-F4 result.

In 1 patient there was overriding with lateral displacement of the distal fragment. Traction and closed reduction failed to improve the position. A Sherman plate was applied. The patient was transferred to another hospital the day after operation, as he had an alcoholic

TABLE 3.—*Fractures of the Upper Third of the Humerus*

Number	Age of Patient	Sex of Patient	Arm	Simple or Compound Fracture	Treatment	Duration of Traction	Duration of Hospitalization	Associated Injuries	Follow-Up	Result: Anatomic	Result: Functional	Comment
24	50	M	R	S	Closed reduction; Blake traction 7-11 lb. (3.2-5 Kg.)	39	42	0	4 yr.	3	4	½" short
38	48	F	R	S	Other injuries	..	..	Concussion; fracture of clavicle, right; ribs 1-10 right, 1-5 left; laceration right lung and pericardium; hemothorax right and left	Died	..	..	Lived less than 24 hours
40	26	M	R	S	Closed reduction; Blake traction; open reduction	8	10	0	.....	..	..	Sherman plate; good reduction; transferred; delirium tremens
53	39	M	L	C	Blake traction 7-10 lb. (3.2-4.5 Kg.)	37	40	Gun shot (2)	0	..	..	No infection
56	40	M	L	C	Débridement; amputation; late traction (Kirschner)	..	..	Gangrene of forearm and hand	.....	..	..	Amputation
60	72	M	L	S	Other injuries	..	1	Fracture of pelvis, ribs (left)	Died	..	..	Bronchopneumonia; lived 20 hours
63	11	M	L	S	Plaster spica	..	21	Solitary bone cyst	3 mo.	4	4	Cyst cured by fracture; pathologic
72	71	F	L	S	Plaster spica 5-7 lb. (2.3-3.2 Kg.)	35	38	0	0	..	..	
81	53	M	L	S	Plaster spica	51	54	0	2 yr.	4	4	Delayed union; operation considered
98	28	M	L	S	Plaster spica 4-6 lb. (1.8-2.7 Kg.); closed reduction; open reduction	12	33	Fracture of left scaphoid ulnar and radial styloids; dislocation carpus	1½ yr.	4	4	Sherman plate
103	39	M	L	C	Blum traction 4 lb. (1.8 Kg.)	44	47	Gun shot	1 yr.	4	4	No infection

TABLE 4.—*Fractures of the Middle Third of the Shaft of the Humerus*

Number	Age of Patient	Sex of Patient	Arm	Simple or Compound Fracture	Treatment	Duration of Traction	Duration of Hospitalization	Associated Injuries	Follow-Up	Result		Comment
										Anatomic	Functional	
3	40	M	L	S	Blake traction 6-7 lb. (2.7-3.2 Kg.)	81	102	Fracture of pelvis, laceration of urethra	7 mo.	3	3	Delayed union; traction discontinued too soon; angulation recurred
4	13	M	R	S	Blum traction 3-3½ lb. (1.3-1.5 Kg.)	37	40	0	1 yr.	4	4	
7	14	M	R	S	Blum traction 2-3 lb. (0.9-1.3 Kg.)	27	32	0	1 yr.	4	4	
9	43	M	R	S	Blake traction 5-7 lb. (2.3-3.2 Kg.)	56	64	Complete fracture of right radius and right ulna, 2d metacarpal (right)	1 yr.	4	4	Slight limitation of pronation of elbow and second finger; plating of radius
41	1½	M	R	S	Closed reduction; plaster	..	17	0	1 yr.	4	4	Kept in hospital for convulsions
45	20	M	L	S	Blake traction 8-10 lb. (3.6-4.5 Kg.)	41	45	0	5 yr.	4	4	
46	47	M	L	S	Blake traction 10-12 lb. (4.5-5.4 Kg.); closed reduction	36	42	Right Colles fracture	1 yr.	4	4	
47	57	M	L	S	Blake traction 8-23 lb. (3.6-10.4 Kg.)	35	40	0	3 mo.	4	3	Still under treatment
48	49	M	R	C	Blake traction 8 lb. (3.6 Kg.)	37	44	Laceration of right hand and forearm	5 yr.	3	3	Abduction 165°
49	56	M	R	S	Blake traction 8-10 lb. (3.6-4.5 Kg.)	39	44	0	4 mo.	4	4	Pathologic fracture; osteitis deformans
51	25	M	R	S	Blake traction 6-8 lb. (2.7-3.6 Kg.)	34	36	0	1 yr.	4	4	
54	54	M	L	C	Other injuries	..	1	Concussion; fracture pelvis, left; calcaneus, dislocation 1st metatarsal	Died	..	..	Lived 7 hours
61	40	M	R	S	Blake traction 5-7 lb. (2.3-3.2 Kg.)	36	49	0	2 mo.	4	3	
64	51	M	L	S	Plaster spica	..	44	0	9 mo.	4	4	Letter; hospitalized because of inability to use crutches
65	31	M	L	S	Blake traction 7 lb. (3.2 Kg.)	6	6	0	0	..	..	Good position in traction; left against advice; psychosis
66	27	M	L	S	Blake traction 5-7 lb. (2.3-3.2 Kg.)	27	35	0	0	..	..	
71	56	M	R	S	Open reduction; tibial graft	..	14	0	0	..	..	Original treatment elsewhere; nonunion
79	40	M	L	C	Blake traction 8-10 lb. (3.6-4.5 Kg.); open reduction	13	47	0	10 mo.	4	4	Temporary radial paresis; Sherman plate; removed 2 mo.
82	11	M	L	S	Blake traction 10 lb. (4.5 Kg.)	29	31	0	0	..	..	A4-F4 result on discharge
83	16	M	L	C	Blake traction 5-10 lb. (2.3-4.5 Kg.)	28	30	Compounded from within	15 mo.	4	4	No operation
87	27	M	L	S	Blake traction 12 lb. (5.4 Kg.)	35	71	Laceration of forearm with infection	1 yr.	4	4	
95	66	M	R	S	Blum traction 4-7 lb. (1.8-3.2 Kg.)	52	57	0	5 mo.	4	4	
105	44	M	R	S	Blum traction 2-7½ lb. (0.9-3.4 Kg.)	38	40	0	5 mo.	4	3	

TABLE 5.—*Fractures of the Lower Third of the Shaft of the Humerus*

Number	Age of Patient	Sex of Patient	Arm	Simple or Compound Fracture	Treatment	Duration of Traction	Duration of Hospitalization	Associated Injuries	Follow-Up	Result		Comment
										Anatomic	Functional	
32	39	M	R	S	Amputation	..	..	Compound crushing fracture radius and ulna at elbow	.....	..	..	Amputation at site of fracture
42	35	M	R	S	Blake traction 8 lb. (3.6 Kg.)	59	72	Right hemothorax; emphysema; fracture right clavicle	6 mo.	4	4	
43	12	M	L	S	Blake traction 5-8 lb. (2.3-3.6 Kg.)	29	33	0	0	..	..	A4-F4 result at discharge
44	51	M	R	S	Other injuries	..	1	Fracture of tibia and fibula right; tibia and fibula left; ribs right 3-10; hemothorax; rupture of liver and spleen	Died	..	..	Lived 11 hours
50	48	F	L	S	Blake traction 10-12 lb. (4.5-5.4 Kg.)	38	42	0	0	..	..	
52	25	M	L	S	Blake traction; open reduction	16	21	0	2 mo.	3	3	Limitation of motion at elbow
55	27	M	L	S	Blake traction 10-12 lb. (4.5-5.4 Kg.)	41	46	Fracture of skull; laceration of brain; 1st dorsal vertebra	0	..	..	
58	39	M	R	S	Open reduction 11/31/28; open reduction 5/8/29	..	..	Nonunion; refracture	.....	..	..	(1) Freeing radial N.; bone chips; (2) inlay tibial graft, union
94	30	M	L	S	Blum traction 5 lb. (2.3 Kg.)	37	42	T fracture; intercondylar	1 yr.	4	3	

psychosis. The reduction obtained was satisfactory. There was no follow-up (case 40).

The other open operation with plating was necessitated by overriding and persistent lateral displacement of the distal fragment. In addition to the fracture of the humerus, the patient suffered a fracture of the scaphoid, a fracture of the radial and ulnar styloid processes and a posterior dislocation of the carpus of the radioulnar joint of the same extremity. Immediate closed reduction of the wrist was performed, together with prolonged immobilization as advocated by Bohler. An A4-F4 result was obtained and the patient was able to continue his work as an expert typist (case 98).

Fracture of the Middle Third of the Shaft.—There were 23 fractures of the middle third of the shaft. The youngest patient was 1 year of age and the oldest 66; the average age was 36. All were male. In 11 cases the fracture involved the right arm and in 12 the left. Two patients were treated by closed reduction and plaster spicas, and 18 by balanced traction (14 by the Blake apparatus and 4 by Blum's method). Open reduction was done for 2 of these fractures, 1 of them being an old fracture with nonunion; in 1 case (case 71) a sliding bone graft from the tibia was used; in the other (case 79), the Sherman plate was employed. Two patients were discharged at their own request.

There were 2 pathologic fractures, 1 caused by an old poliomyelitic infection and the other by osteitis deformans.

There was 1 death, seven hours after admission, from associated injuries.

Traction was maintained for the longest period (eighty-one days) in case 3. The patient was taken out of traction too soon, with resulting angulation, as union was not solid. Therapy in each case must be individualized. Standardized treatment will result in many failures.

There were 4 compound fractures. Two were compounded from without, 1 occurring in the patient who died. The other 2 were compounded from within. The 3 survivors were treated conservatively, and the fractures healed without infection.

Fourteen patients were treated with Blake board traction; of these, 7 presented A4-F4 results, 2 presented A4-F3 results, 1 presented an A4-F4 result on discharge and the results for 2 are unknown.

Four were treated with Blum board traction; of these, 3 presented A4-F4 results and 1 presented A4-F3 result.

Two were treated with closed reduction and plaster spica. Both presented A4-F4 results.

Two were treated with open reduction; of these, 1 presented an A4-F4 result. The result for the other is not known.

There was 1 death.

Fracture of the Lower Third of the Shaft of the Humerus.—There were 9 fractures involving the lower third of the shaft. Eight patients were male and 1 female. Five fractures resulted from traffic injuries, 2 from falls on the street, 1 from a fall from a height, and 1 from other injury. Four were on the right and 5 on the left side. None were compounded. Five were treated by traction (4 by Blake and 1 by Blum traction). One was an old fracture with nonunion and paralysis of the radial nerve, which had been operated on elsewhere with retention by kangaroo tendon. Two operations were performed, the first freeing the radial nerve and freshening the bone ends. Seven months later the bone was refractured and plated at a second operation. There was no nerve paralysis and union was obtained. The follow-up period was three months.

In 1 case amputation was done on admission because of compound crushing fracture of the forearm with involvement of the elbow joint.

Four patients had associated injuries; of these, 1 died eleven hours after admission.

Open reduction was performed in 1 case in addition to the case of nonunion, the fragments being retained with a Sherman plate. Union was obtained with moderate deformity, and flexion of the forearm was limited to 90 degrees.

Of the 5 cases in which traction was used the results of treatment in 2 are unknown, except that union was present on discharge.

Two patients treated with Blake traction presented A4-F4 results.

One patient with a T fracture treated by Blum traction showed an A4-F3 result after one year.

CONCLUSIONS

Fracture of the surgical neck frequently results in partial loss of abduction and external rotation. From a review of cases of this condition it is obvious that traction-abduction is not effective in overcoming anatomic displacement, and indeed often results in increased deformity, i. e., angulation with the apex medial. From the point of view of displacement it is obviously preferable to place the distal fragment in alinement with the proximal fragment, which would eliminate abduction at 90 degrees in the majority of cases. The only valid argument for traction-abduction for fracture of the surgical neck (excluding fracture in which the upper fragment is abducted) is the preservation of abduction and external rotation. I have not had sufficient experience with other methods to answer that question finally, but I believe that the difference in results is not sufficient to justify its continuance, except where it is warranted by the position of the upper fragment. I propose to try a modification of the Henderson splint with an adjustable hinge for varying degrees of abduction and ambulatory treatment in such cases. In addition to the advantages of mobilization, it would greatly reduce the expense both to the patient and to the hospital. In cases of

fracture of the surgical neck, nonunion is so rare as not to deserve consideration in the choice of treatment.

Nonunion is an important consideration in cases of fracture of the shaft. W. C. Campbell [3] wrote that "delayed union and non-union occur more often in fractures of the shaft of the humerus than in any other long bone." Von Bruns reported that of 1,274 ununited fractures, 376, or 30 per cent, were fractures of the humerus, and of 681 cases of pseudarthrosis, 226, or 33 per cent, involved the humerus. Codvilia, Cuneo and Sutro found 32 per cent of cases of pseudarthrosis of the humerus as against 13 per cent of cases in which the condition involved the tibia.[4] Including 41 cases reported by Colp and Findlay during 1926 and 1927 there have been no known instances of nonunion in fracture of the shaft of the humerus in 82 patients treated primarily at the Beekman Street Hospital.[5] This would indicate that for fracture of the shaft traction-abduction treatment is an effective method of immobilization.

It is especially successful for fracture of the middle third and to a slightly less extent for fracture of the upper third. Results have been least satisfactory for the lower third, but they are based on comparatively few cases. Fracture of the lower third of the shaft is difficult to treat by any method. It would seem that for such a fracture, when anatomic reduction is not promptly obtained by traction, open operation should be resorted to. It is evident, however, that in the presence of a comminuted fracture or a T fracture the operator's skill will be taxed to the utmost to avoid impairment of the elbow joint.

The use of traction should be combined with closed reduction, and when reduction is successful osseous union should occur. The addition of closed reduction is particularly necessary for transverse fractures. Delayed union will result in nonunion if immobilization is not continued until fusion occurs. Its duration should allow for individual variation in the length of the period of healing.

It is desirable that a prompt decision should be made whether to persist with closed methods or resort to open operation. It should be possible within a week to arrive at such a decision. Some of my results with open reduction would have been better if this decision had been made earlier. It makes operative treatment easier and results in a shorter period of disability and a better functional result for the patient. Calcification of callus and the late softening of the cortices of the bones due to decalcification vitiate the operative results in cases in which treatment is delayed.

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ONLAY BONE GRAFT FOR UNUNITED FRACTURES

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After using methods commonly employed for nonunion, with varying degrees of success, and after observing the method of Henderson, approximately twenty years ago I began to use the massive onlay graft. It was apparent that two factors are necessary to obtain a high percentage of excellent results in cases of nonunion: (1) absolute fixation and (2) promotion of osteogenesis (callus formation). In 1932 I presented in the ARCHIVES OF SURGERY an analysis of 125 operations. Since that time 136 additional operations have been performed, and a supplementary report is appropriate.

There is no arbitrary time for consolidation of a fracture; much depends on the degree of injury to the extremity, the soft structures involved and the efficiency of treatment. Often when union has not occurred after the lapse of sufficient time, more efficient fixation, with or without functional use of the part, may induce solidification. An ununited fracture is one in which there has been sufficient organic change to render osseous union either impossible or exceedingly improbable. No arbitrary statement can be made as to the time at which a fracture may be designated as permanently ununited, although if there has been no progress toward union at the end of six months one is justified in making the diagnosis of nonunion. There are undoubtedly instances, however, in which union has occurred after a much longer period, and not infrequently nonunion may be apparent at an earlier time. In any discussion of this subject, distinction must be made between delayed union and nonunion. In many instances this is not done; therefore, many of the data are unreliable.

In the treatment of nonunion certain inefficient methods are commonly employed and may be enumerated as follows: (1) denuding of osseous surfaces and maintaining approximation with absorbable and nonabsorbable suture (catgut, kangaroo tendon and wire); (2) application of steel and beef bone plates or pegs; (3) plastic "step-up" or dovetailed wedging of the fragments; (4) drilling of fragments, and (5) application of various types of inefficient bone grafts, such as chip grafts, Delangeniere grafts and intermedullary grafts. Such operations are performed in a high percentage of cases of ununited fracture. Union is induced in some instances by such measures, but the question

is not what nature will occasionally accomplish but by what means osseous fusion can be secured in the highest percentage of cases. With merely delayed union, consolidation can often be more rapidly induced by simple drilling of the fragments or other methods of stimulation of callus; for true nonunion, however, such measures should be discarded, as the percentage of failures is entirely too high.

For 213 patients I have employed the massive onlay bone graft on 261 bones with nonunion. The mechanical principles of this method are similar to those of a procedure employed by Henderson and were originally devised after observation of it. They differ, however, in the following respects: 1. A plain, flat surface is made for the reception of the graft, with as little removal of bone from the fragments as possible. 2. Cancellous bone is employed to promote osteogenesis as an intermedullary graft and is generously packed around the site of the fracture. 3. The endosteum is removed from the graft, the cortical portion only being utilized for fixation as well as for osteogenic purposes. 4. The graft is fixed with autogenous bone pegs instead of beef bone screws.

The details of the procedure are as follows: An ample incision is made over the point of fracture, with sharp and blunt dissection between the muscular and fascial planes to the site of the fracture, which is exposed. All intervening scar tissue is excised (fig. 1). An incision is made through the periosteum of each fragment for several inches, depending on the length and anatomic location. The periosteum is stripped from ½ to ¾ inch (1.3 to 1.9 cm.) from the circumference, the soft parts from which circulation is derived being left attached as much as possible. If there is malposition the fragments are rotated until the normal relation has been restored. If there is perfect apposition the ends of the fragments need not be disturbed, but this is comparatively rare. The fragments are pared with a chisel or a motor saw, and each medulla is reamed out (fig. 2) until normal marrow tissue is removed. With a chisel, "shavings" are removed from the circumference until there is a continuous flat surface for 3 or 4 inches (7.5 to 10 cm.), when possible, on each fragment. A broad, flat, massive graft is taken from the tibia. It should be of sufficient dimensions to assure firm fixation. With a motor saw the graft is split longitudinally through the edge or small diameter into two parts, a strong outer plate, consisting of dense bone or cortex, and an inner layer, the endosteum. A strip of endosteum is placed within the medulla, bridging the site of the fracture as reduction is made, normal marrow tissue rich in osteogenetic potentiality being thus restored. From the outer plate, or as a separate graft, a strip of dense bone (fig. 3) is taken, from which are made six or eight autogenous bone nails of appropriate size. This is accomplished

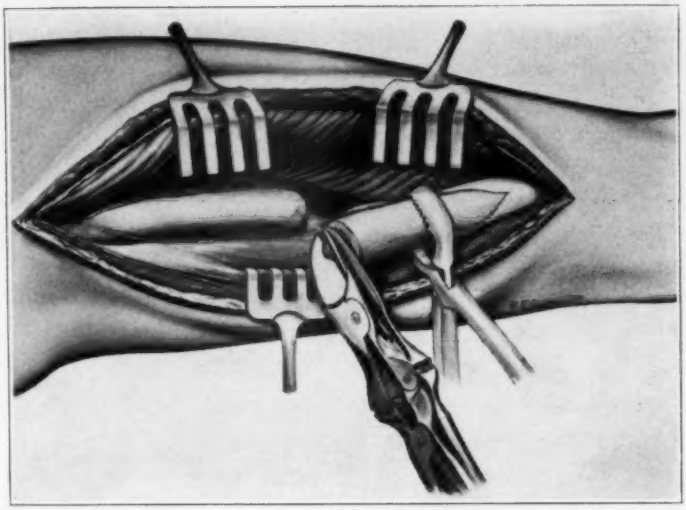

Fig. 1.—Removal of intervening fibrous tissue and freshening of the ends of the bones. The bone is stripped of as little periosteum as possible.

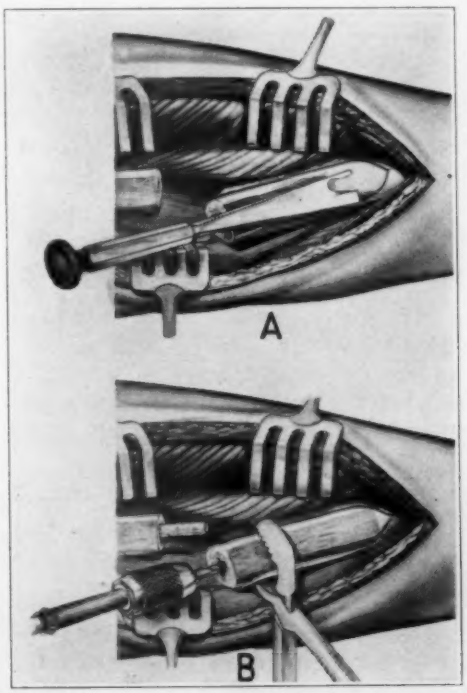

Fig. 2.—*A*, removal of "shavings" from the circumference until there is a continuous flat surface for three to four inches on each fragment. *B*, reaming out of each medulla. A strip of endosteum is placed within the medulla as the fracture is reduced.

by the aid of a rotary file (attached to the motor saw) and a metal gage to measure dimensions. The strong outer plate is held to the flat surface of the bone, passing across the site of fracture. Three or four drill holes are made through the graft and through each fragment, into which the autogenous bone nails are driven. Care should be taken not to place the autogenous pegs close to the site of fracture. The remainder of the endosteum is broken into small particles and placed with the "shavings" about the site of fracture.

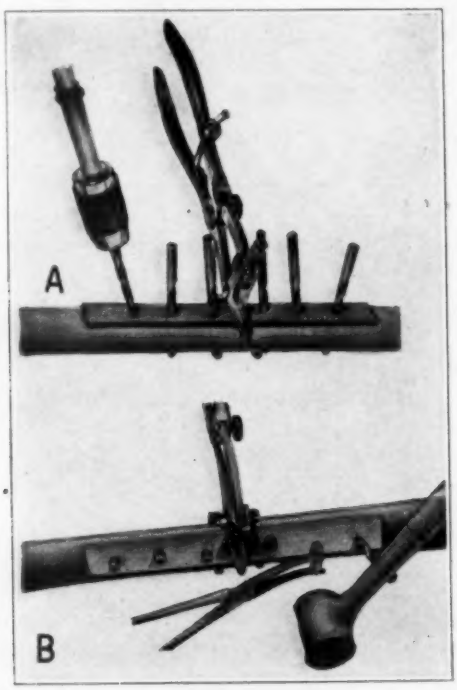

Fig. 3.—*A*, graft consisting of dense bone or cortex with drills in place. *B*, autogenous bone nails of appropriate size inserted into drill holes.

Spongy bone from the upper end of the tibia is always available and can be obtained by a sharp bone curet (fig. 4). About six pieces are removed in this manner and applied around the area of fracture. A graft of spongy bone is more proliferative than any other type of graft, being successful in 100 per cent of cases in an operation which I have devised for a type of paralytic drop foot. By this method solid fixation is attained, so that when the operation is complete no motion is apparent. Transplantation of endosteum to the medulla and cavernous bone about the fracture is an excellent method of promoting osteogenesis.

After-treatment consists in complete fixation by a plaster of paris cast or an efficient splint, which remains for a period of eight weeks. When this is removed, a convalescent splint is applied, usually in the form of a leather corset to reproduce the cast. Joints are usually incorporated, so that active and passive motion may be carried out as soon as is feasible. The brace is used until there is no doubt as to complete consolidation. The period is usually from two to four months, depending on the local condition in the case in question. Active motion may be instituted at the end of two to three months. One patient for whom this procedure was employed in both bones of the forearm left the hospital without permission at the end of twenty-four hours after operation. After a few weeks he removed the cast but obtained solid union

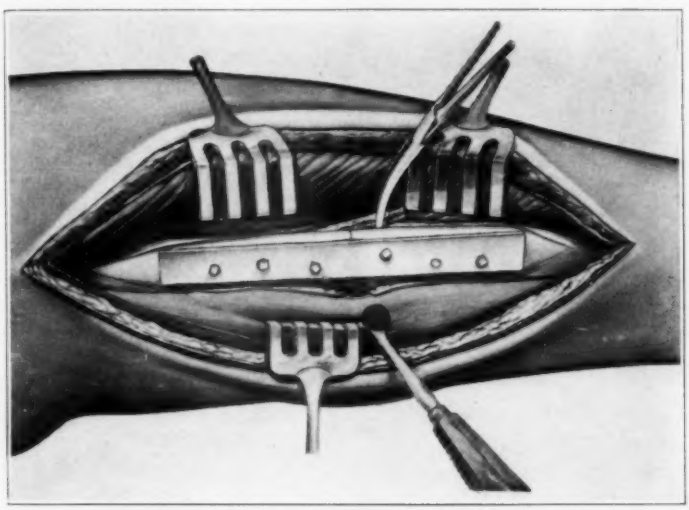

Fig. 4.—Cancellous bone from the upper end of the tibia, placed adjacent to the fracture site.

and excellent function. However, the process of bone repair, which is decreased in all fractures with nonunion, must be carefully guarded until complete consolidation occurs. Also, fracture of a bone graft with relapse to the former state of nonunion is not infrequent after the use of inefficient methods, especially the intermedullary graft. In 1 case in which I employed the intermedullary graft over twenty years ago for an ununited fracture of the lower end of the ulna, there was apparent union, but after six months there was refracture from a slight blow, and a return to the former status of nonunion occurred. In a case of ununited fracture of the humerus recently observed, there was a history of solid union after a large intermedullary graft, with refracture six months after operation, induced during swimming.

Another important factor is that the graft must not be applied under tension or there will be gradual dissolution at the point of tension. This has been observed in bone grafts to the spine which were employed under tension to conform to kyphosis or when kyphosis has occurred after the graft was employed.

Fig. 5.—Nonunion of the humerus.

The graft under discussion is a massive onlay graft and must be efficiently applied as described; otherwise the procedure is a caricature of the correct operation. Frequently, illustrations in the literature have demonstrated that this method has been inadequately employed. Excellent results obtained by the method have been reported by Dr. Barnett Owen of Louisville, Ky., Dr. Kelly West of Oklahoma City, Dr. J. S. Norman of Pueblo, Colo., and (in personal communications) Dr. John Wilson of Los Angeles and others.

The importance of complete internal fixation as described has been demonstrated by others in reports of excellent end results. Albee has employed the inlay method and has claimed that he can secure complete

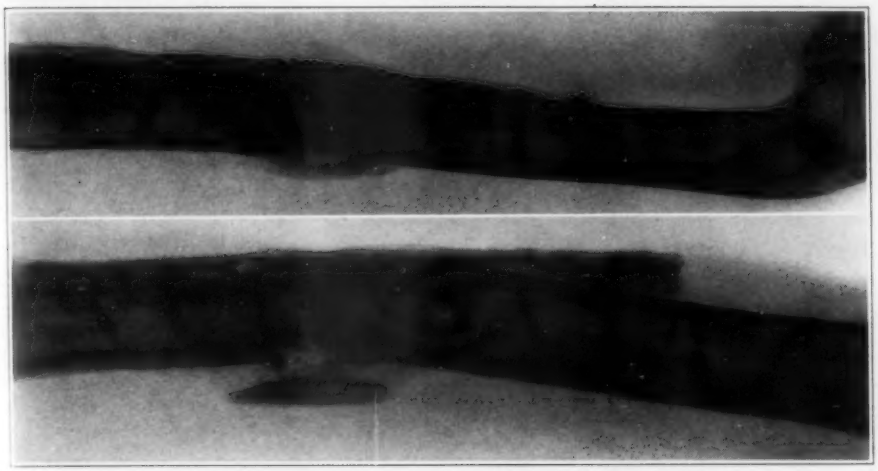

Fig. 6.—Fracture shown in figure 5, three months after onlay bone graft.

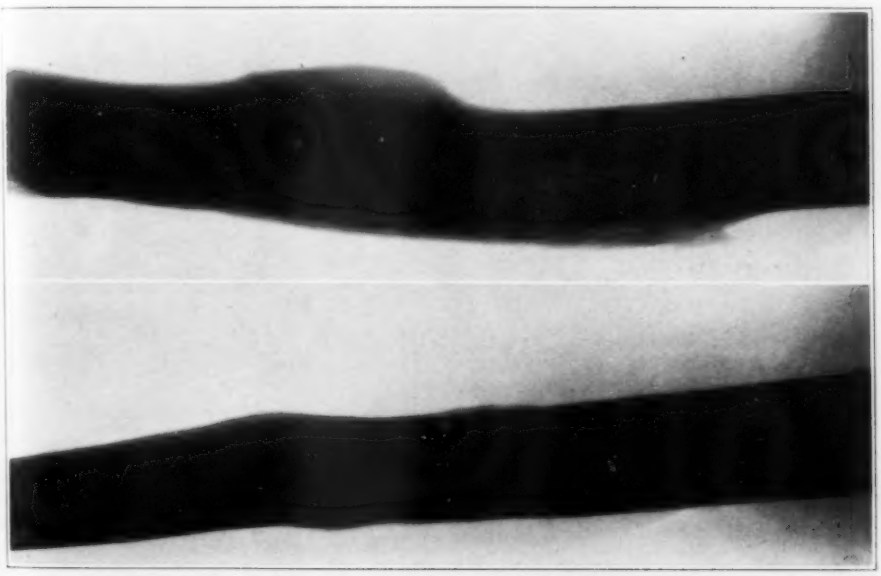

Fig. 7.—Fracture shown in figure 5, six years after onlay bone graft. Note increased dimension and strength of bone as obtained by the onlay method.

fixation, but I was unable to secure this after many attempts. Gill stated that he removes a massive graft of one-half the circumference of the bone and employs it as a graft across the line of fracture, which

is solidly fixed with steel screws. O'Neill Sherman stated that he employs a massive graft from the tibia, which is fixed within the medullary cavity across the line of fracture by steel screws. These methods have the disadvantage of removal of a large portion of the circumference of

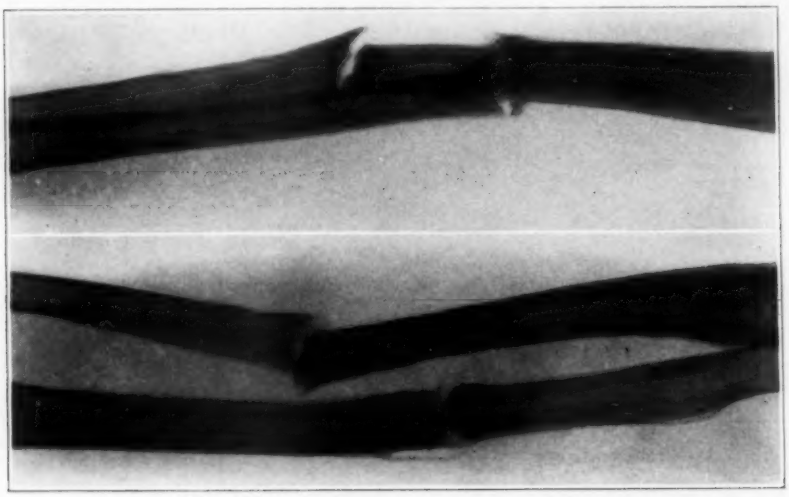

Fig. 8.—Nonunion of both bones of the forearm.

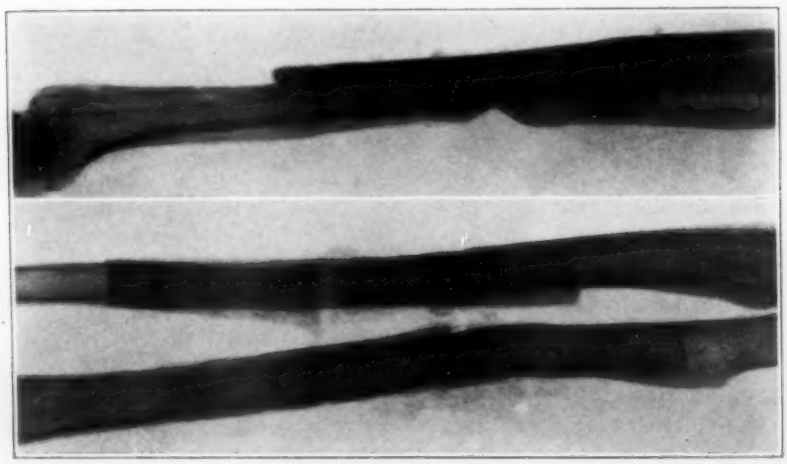

Fig. 9.—Fracture shown in figure 8, five months after onlay bone graft.

the fragments from which union is finally to be secured. In case of infection with extrusion of the graft, there is loss in the circumference and at times in continuity, and the chance of success by subsequent procedures is decreased.

Recently, Bennett has reported success in 10 cases of fracture of the humerus, treated by a method which consists of making long oblique fragments, after which beef bone nails are employed to transfix the fragments. The disadvantage of this method is that the arm is definitely shortened. I reported the same procedure for oblique ununited fractures, with the exception that autogenous nails were employed. However, nonunion of oblique fractures is exceedingly rare.

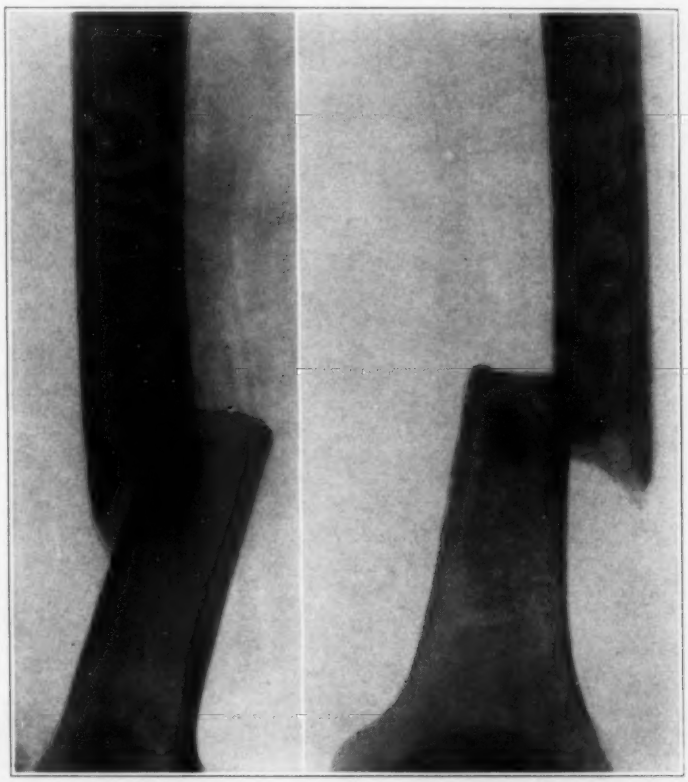

Fig. 10.—Nonunion of the femur.

Harkins and Phemister have advanced as criticisms of the massive onlay graft that the procedure carries some risk of infection and in the case of long bones, particularly the femur, of hemorrhage and shock, and that resection of the fragment ends results in shortening of the bone to an objectionable extent. These have not proved to be serious objections in my experience. In this series there were 31 cases of infection. In 29 the infection occurred in a compound fracture; in all but 2 cases it could be attributed to the relighting of a previous pyogenic infection. No undue shock or excessive shortening has occurred. With these objec-

tions in mind, Harkins and Phemister advised laying onlay grafts across the fracture line without fixation and without disturbing the site of fracture to any appreciable degree. This method was devised only for cases of nonunion in which displacement is not marked.

ANALYSIS OF CASES

In 1932 an analysis of the end results in 104 cases was made, and the same plan will be employed on this occasion for 261 bones of 213 patients.

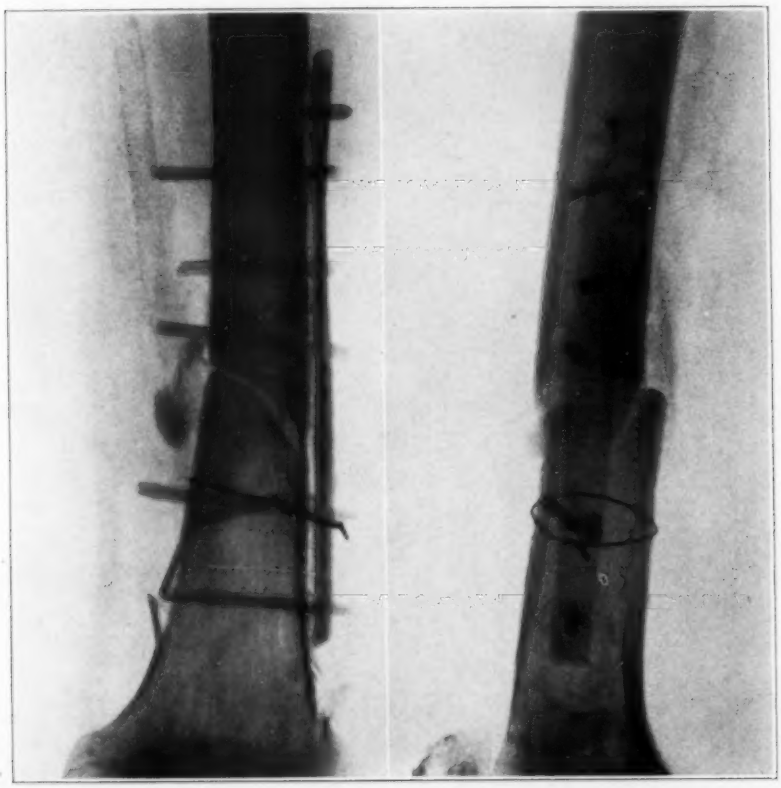

Fig. 11.—Fracture shown in figure 10, two months after onlay bone graft.

When bone grafts were employed as entirely separate surgical procedures for nonunion of two bones of the same patient, for example, the radius and the ulna, the procedures were listed as two operations, as each was a separate surgical equation. Similarly, failures have been counted in the same manner. When a bone was regrafted, as occurred in 5 instances in this series, two operations were reported, one as a failure and one as a success. Hence the apparent discrepancy between the number of patients and the number of operations.

END RESULTS OF TWO HUNDRED AND SIXTY-ONE OPERATIONS

Number of operations	261
Number of patients	213
Males	180
Females	33
Ages (5 to 62)	
Patients under 20 years of age	20
Patients above 50 years of age	15
Solid union	15
Length of time since fracture	4 mo. to 8 yr.
Approximate average length of time since fracture	14 mo.
Cases in which there had been 1 to 4 previous operations	58
Gunshot or compound fractures	55
Failures in cases with history of compound fracture	7
Time elapsed too short to permit determination of union or result unknown	10
Failures	16
Regrafting performed for failures	5
Solid union	5
Solid union, total	235
Percentage of instances of solid union induced in 251 operations	93.6

POSTOPERATIVE INFECTIONS

Number of cases	31
Osseous union induced	24
Sequestration of part of or entire graft	24
Failure of union after sequestration	7
Cases with history of previous pyogenic infection	24
Compound fractures without infection	5
Simple fractures	2

RESULTS OF ONLAY GRAFTS IN DIFFERENT REGIONS

Tibia

Number of operations	59
Solid union	54
Failures	5
Percentage of instances of solid union	91.5

Humerus

Number of operations	60
Solid union	57
Failures	3
Percentage of instances of solid union	95

Femur

Number of operations	36
Solid union	33
Failures	3
Percentage of instances of solid union	91.6

Radius

Number of operations	23
Solid union	22
Failures	1
Percentage of instances of solid union	95

Ulna

Number of operations	15
Solid union	14
Failures	1
Percentage of instances of solid union	93

Radius and Ulna

Number of operations	58
Solid union	55
Failures—(radius 1, ulna 2)	3
Percentage of instances of solid union	94

The chances of success with bone grafts are thought to be less when patients are of advanced age, but it is interesting to note that in this series in the 15 patients above the age of 50 the grafts were 100 per cent successful. In the oldest patient, aged 62 (a patient not included in this report was 72), nonunion had existed for seven months. Not only did union occur uneventfully after operation, but the patient was able to return to his former occupation, as a laborer on the railroad. Of the 251 ununited fractures, 55, or approximately 22 per cent, were

Fig. 12.—Nonunion of the tibia.

compound or gunshot fractures, which is surely suggestive, if not absolutely conclusive, that compound fractures have a definite causative relation to ununited fractures. Of the 55 ununited fractures which had been originally open or compound, there were 7 in which union failed to be induced. Only those in which there was frank pus with definite constitutional symptoms of pyogenic infection are considered as presenting infection. Union was induced regardless of an intense infection in 24 of the 31 cases in which infection was present. In 7 the graft remained intact, while in 24 there was sequestration of a part of the transplant.

In 17 of these 24 cases, regardless of sequestration, the graft functioned for sufficient time to induce union.

In this series there were 16 cases in which the onlay method failed to produce union. In 2 cases of nonunion of both bones of the forearm, fusion was induced in the ulna but not in the radius; function, however, for each patient was so satisfactory as compared with the former status that further operative measures were declined. The causes of the 16 failures may be analyzed as follows: Eight were due to technical errors

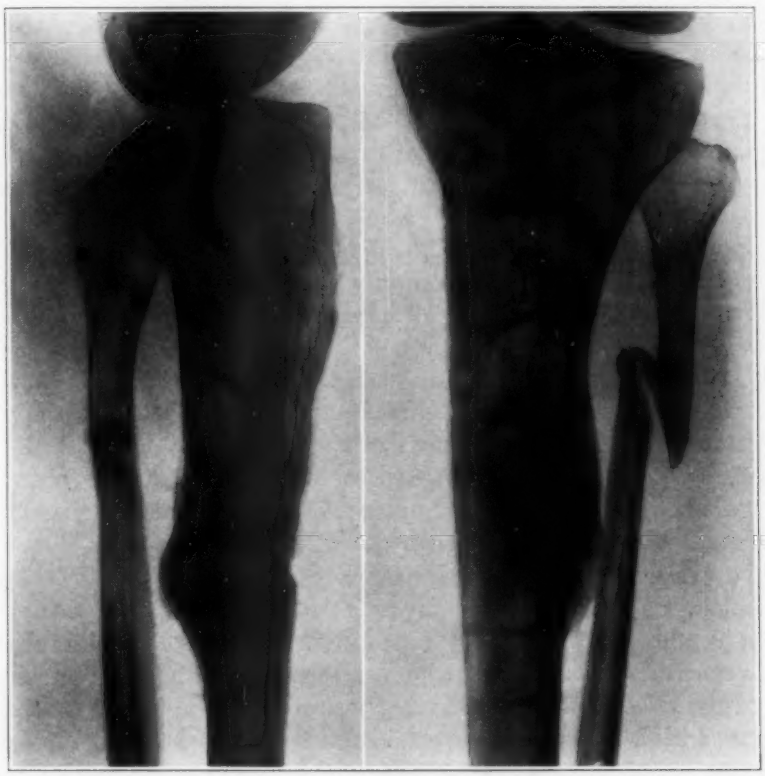

Fig. 13.—Fracture shown in figure 12, six months after onlay bone graft.

(fracture of the graft, poor approximation of the fragments or separation of the graft from the fragment); 7 were due to infection and sequestration; 1 was due to lack of osteogenesis, possibly constitutional. In 5 of these cases regrafting was successfully done.

A careful review has been made of serial roentgenograms at intervals of approximately thirty to sixty days for the first six months, and in many cases for two years. When there was satisfactory application, as denoted by close contact of the graft fragments, there was no change in density or structure of the graft, which apparently fused to the host,

increased in size and became gradually assimilated. The bone nails gradually disappeared, but there was usually permanent evidence of the graft, as denoted by an increase in diameter of the shaft. In cases with extensive atrophy of bone, union was secured, though delayed, evidently because of the fact that fixation was not as firm. In many, proliferation of the transplanted endosteum and spongy bone about the site of fracture was apparent by the end of eight weeks. In a small number, satisfactory approximation was not maintained between the graft and the shaft of the bone over a portion of the graft. In these there was definite evidence of absorption and distintegration, as denoted by enlargement of the drill holes and punched-out areas in the graft where it was not in contact. At those parts in which there was approximation, however, the integrity of the graft was not involved, and fusion continued. This did not apparently affect the end result, as fixation was secure except that it was thought necessary to continue the use of external apparatus for a longer period.

When there was a primary infection or an old infection was relighted by operation, gradual disintegration with absorption of a portion of the graft or all of it was noted in 24 cases; often there was also evidence of new bone formation, especially along the line of the fracture, where endosteum and spongy bone had been transplanted. Fixation, however, was usually maintained for a sufficient time to permit osseous union of the fracture, so that the function of the graft was accomplished. The graft, or a portion thereof, in such cases acted partly as a foreign body, but it is believed that an autogenous graft, even though infected, is better tolerated by the tissues than is foreign material.

In a small number of cases the wound failed to heal by primary intention, as evidenced by persistent drainage for several weeks. Whether the condition in these cases should be classed as mild infection or as caused by undue hemorrhage from the bone with persistent seepage of serum is a moot question. At any rate, such a condition is often observed after an extensive operation on bone. In this type of case the roentgenogram demonstrated disintegration of the graft, similar to the changes previously described as occurring in cases in which mechanical approximation was not obtained. Also, such changes were occasionally seen when there was primary healing of the wound, but in by far the greater number of cases the graft apparently assumed an active part in physiologic bone construction.

Union of ununited fractures is secured by two different processes: functional adaptation of the graft, as may be denoted by hypertrophy, and union of the fragments themselves. Fractures of the graft have occurred when protection was not sufficient or when there was undue tension on the graft or drill holes too near the fracture site, owing to

an error in surgical technic, but always within a period of three months. In those instances in which osteogenesis is exceedingly deficient in the fragments, union must be accomplished largely by graft alone, with gradual fusion of the fragments by a process of functional adaptation along the lines of stress. In such cases protection must be continued for a longer period. In most instances union is induced between the fragments, but it is much slower than in fresh fractures; therefore, it required the services of a graft which in addition to promoting osteogenesis is able to hold the fragments absolutely fixed.

CONCLUSIONS

1. Union is accomplished in a shorter time by the massive onlay transplant than by other operations generally used, as evidenced by the fact that no motion can be detected from the time the operation is completed.

2. Earlier movement is permitted in adjacent joints, and thus function is conserved.

3. The onlay graft actually increases the dimension and strength of the bone; the circumference is maintained intact. Practically no bone is excised, but new bone is added.

4. Of 31 patients with postoperative infection, 24, or 77.4 per cent, showed solid union.

5. Solid union was secured by means of the onlay graft in 235, or 93.6 per cent, of 251 cases.

6. The criticism has been made that the operation is too technical or difficult, requiring a well trained team of at least two experts and three assistants, but the means are surely justified if the percentage of good results can be materially increased thereby.

ORAL ADMINISTRATION OF METHYL-CHOLANTHRENE TO MICE

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Experiments to produce cutaneous carcinoma by application of tar and, more recently, of the several synthesized carcinogenic compounds and to produce sarcoma by subcutaneous or intramuscular injection of these substances have been repeatedly performed on mice, rats, rabbits and guinea pigs. A significant percentage of pulmonary tumors has been observed as a result of cutaneous application of the compounds. However, relatively fewer observations have been published on the production of "internal cancers" by causing the animals to ingest the various carcinogenic agents in one form or another.

By repeated tarring of the mouths of 50 rats Bonne[1] produced benign papillomas in the skin of the face about the mouth and also squamous cell carcinomas in the buccal cavity, the esophagus and the cardiac end of the stomach. Voronoff and Alexandrescu[2] administered a mixture of tar, hydrous wool fat, aniline oil and toluylenediamine by mouth to 10 rats and observed 1 papilloma of the tongue and 1 carcinoma of the stomach. A number of negative reports from oral administration of tar have been made by other observers. Reinhard and Candee[3] did not observe benign or malignant tumor formation in mice fed dibenzanthracene mixed with butter, during a period of seven months. Ilfeld[4] inserted dibenzanthracene pellets into the gastric wall of a dog and pellets of benzpyrene under the gastric mucosa of 6 ferrets, with negative results after one year. Oberling[5] also obtained negative results after feeding benzpyrene to rats and mice for periods of six to ten months. On the other hand, Waterman[6] observed carcinomas of the

This work was facilitated by a grant from the Cancer Research Institute of the Chicago Woman's Club.

From the Department of Surgery and the Division of Roentgenology of the Department of Medicine, University of Chicago Clinics.

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2. Voronoff, S., and Alexandrescu, G.: Néoplasmes **8**:129, 1929.
3. Reinhard, M. C., and Candee, C. F.: Am. J. Cancer **26**:552, 1936.
4. Ilfeld, F. W.: Am. J. Cancer **26**:743, 1936.
5. Oberling, C., and others: Bull. Asoc. franç. p. l'étude du cancer **25**:156, 1936.
6. Waterman, N.: Acta brev. Neerland. **1**:18, 1937; abstracted, Am. J. Cancer **30**:379, 1937.

stomach, 4 with metastases, in 5 mice which had been fed several milligrams per day of benzpyrene in lard for periods varying from one hundred and twelve to three hundred and thirty-six days.

We obtained negative results from feeding dibenzanthracene in lard to white mice three times a week for six months. (These mice were from the same colony as those to be described.) Recently Rowntree and his associates [7] observed multiple intra-abdominal spindle cell sarcomas in rats fed crude wheat germ oil. No epithelial neoplasms were reported. Yoshida [8] induced carcinoma of the liver in rats by feeding 2-amino—5 azotoluene. Otsaka [9] observed papillomatosis in the fundi of the stomachs of mice fed diazoaminobenzene.

TABLE 1.—*Results of Experiment 1*

Mouse	Period of Methylcholanthrene Administration Days	Necropsy
BW 1	164	Marked emaciation; small, rounded pedunculated papilloma approximately 1.5 mm. in diameter in fundus of stomach; microscopic section not obtained
BW 2	168	Large fusiform mass about right mandible, with extension into neck; flat grayish ulcer along right gum margin; microscopic examination showed squamous cell carcinoma arising over right gum with secondary invasion of mandible and direct extension into neck
BW 3	169	Squamous cell carcinoma 0.5 cm. in diameter arising in skin of the chin and not connected with the mucosa of the lower lip; large ulcerating carcinoma of left anterior breast
BW 4	169	Several small benign epithelial papillomas on chin; large ulcerating carcinoma of second left breast
BW 5	178	Benign papilloma of skin of right mandible; ulcerating carcinomas of the left anterior 2d and 3d breasts with pulmonary metastasis
BW 6	175	Benign squamous cell papilloma in upper portion of stomach where mucosa is squamous epithelium; carcinoma of 2d left anterior breast; squamous cell carcinoma of skin of right side of neck; nonmalignant chronic ulcer on right side of nose
BW 7	186	No tumor
BW 8	186	Squamous cell carcinoma 0.6 cm. in diameter on right side of chin; nonneoplastic ulcer just to the left of this

Because methylcholanthrene, one of the most potent carcinogens, is chemically related to bile acids [10] and because bile or its decomposition products normally bathe a large portion of the alimentary canal, the following feeding experiments with this substance were performed.

EXPERIMENT 1.—Fifteen white mice of unknown genetic history, obtained from a commercial dealer's inbred colony and at least 6 months old, were given 2 minims (0.12 cc.) of a 1 per cent solution of methylcholanthrene in olive oil three times a week. To prepare this solution it was necessary to heat the olive oil prior to admixture with the substance; as the olive oil cooled the methylcholanthrene did not crystallize out of solution. The mice were held firmly back downward while the material was forced into the mouth by means of a glass dropper. Some of it was swallowed

7. Rowntree, L. G., and others: Am. J. Cancer **30**:359, 1937.
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immediately; some remained in the mouth for a short period, and some spread over the face, the neck and the anterior portion of the thorax. Eight mice survived for the duration of the experiment, approximately six months. In those dying after shorter intervals, no lesions were observed at necropsy.

The animals were killed as they became weak and emaciated and apparently would die in a few days. The results are recorded in table 1.

Observations on large numbers of mice obtained in the course of other experiments and procured from the same dealer's stock showed that in

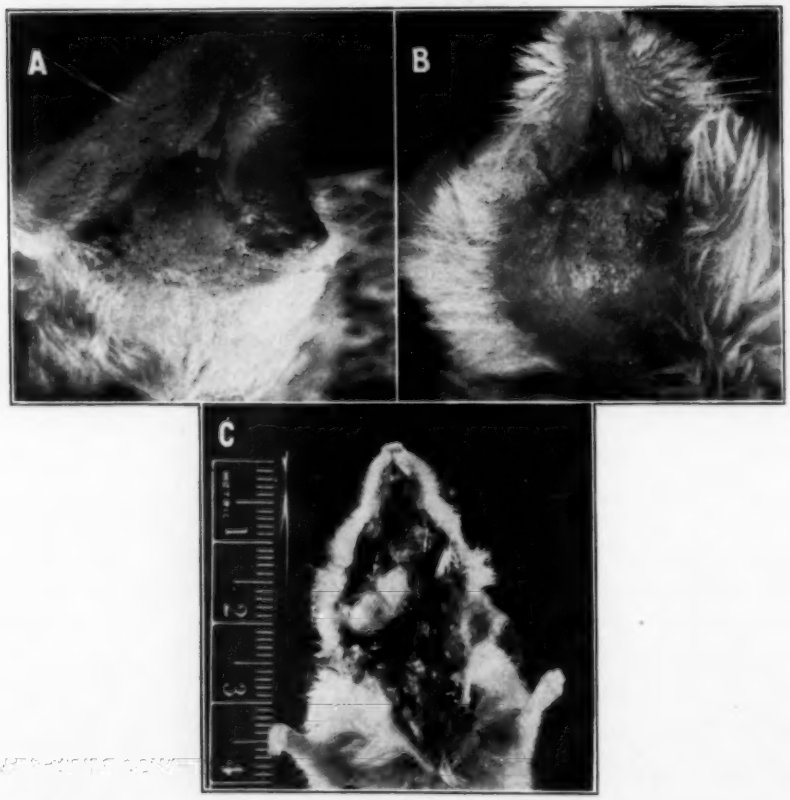

Fig. 1.—*A* (mouse BP1), squamous cell carcinoma of the left angle of the mouth, involving the inner aspect of the left cheek of a mouse fed methylcholanthrene over a period of sixty-seven days. The photograph was taken twenty-two days after the first appearance of the lesion. *B*, large swelling over the right mandible and the floor of the mouth, caused by a squamous cell carcinoma arising in the mucosa over the right mandible and spreading over the floor of the buccal cavity. The photograph was taken one hundred and sixty-eight days after feeding with methylcholanthrene was started. (Mouse BW2.) *C*, large squamous cell carcinoma arising in the right wall of the hypopharynx, extending outward to the base of the right ear. The photograph was taken one hundred and forty days after the beginning of the experiment. (Mouse BP2.)

Fig. 2 (mouse BW2).—Photomicrograph of a squamous cell carcinoma of the mucosa over the right mandible, showing invasion of the latter and infiltration about the tooth (*T*). *M*, normal buccal mucosa. *C*, infiltrating carcinoma.

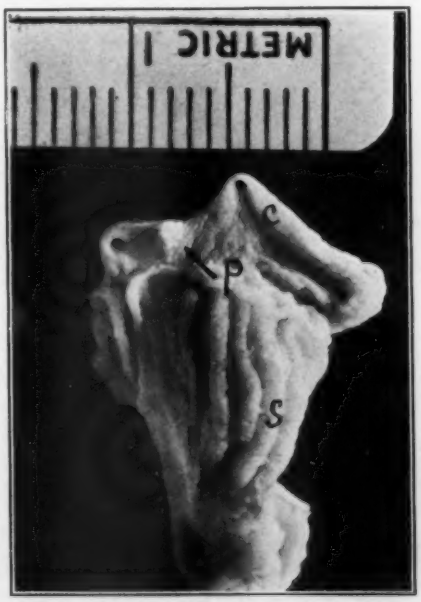

Fig. 3.—Stomach of mouse killed one hundred and sixty-four days after the beginning of the experiment. *C*, forestomach, lined by stratified squamous epithelium. *S*, midportion and pyloric portion, lined by typical gastric mucosa. *P*, benign squamous cell papilloma.

15 to 20 per cent of the females of this strain spontaneous mammary tumors developed. Of the 7 animals for which positive results were obtained in the aforementioned series, 4 had carcinoma of the breast after at least one hundred days from the beginning of the experiment. While it is probable that these tumors were not related to the applications of methylcholanthrene, it must be pointed out that all of the mammary tumors arose well forward on the thorax, an area over which the oil solution spread at each intra-oral application.

Fig. 4 (mouse BW6).—Photomicrograph of a benign squamous cell papilloma in the cardiac portion of the stomach.

EXPERIMENT 2.—Methylcholanthrene was dissolved in lard to make a 1 per cent solution by weight. By means of a small glass syringe and a filed-off 18 gage needle, 2 minims (0.12 cc.) of the mixture was injected into the mouths of the animals every other day for four months. The administrations were then reduced to twice a week. The material was injected slowly in order that the animals might immediately swallow as much as possible. In contrast to the first experiment, a relatively small amount of the substance escaped over the face and anterior part of the body. Of a total of 33 animals, positive results were observed for only

2. Many of the animals became toxic in the earlier weeks of administration and died. The longest survivor lived one hundred and sixty days. The positive results are summarized in table 2. Complete autopsies were done on all animals. There were no papillomatous or other lesions in the stomachs or intestinal tracts in any of the animals examined in the second group.

TABLE 2.—*Results of Experiment 2*

Mouse	Period of Methylcholanthrene Administration Days	Necropsy
BP 1	67	Small rounded carcinoma at left angle of mouth, increasing in size to 89th day, when it measured 8 mm. in diameter; animal died spontaneously; lesion involved the mucosa of the cheek as well as the skin on the outer aspect; microscopic examination showed squamous cell carcinoma
BP 25	140	Animal died spontaneously; on the right side of the hypopharynx and extending through to the base of the right ear there was an oval firm whitish mass 15 by 8 mm.; microscopic examination showed squamous cell carcinoma

COMMENT

From these experiments it would appear that although methylcholanthrene, as has been stated, is chemically related to bile acids, it does not exhibit a marked degree of potency on oral administration as regards induction of neoplasms even in the upper regions of the alimentary canal, where the lining is stratified squamous epithelium. Failure to produce lesions in the glandular epithelium of the lower part of the stomach and in the intestines might, in addition to a high degree of resistance on the part of such epithelium, be explained by certain mechanical factors. Whereas in cutaneous application and subcutaneous injection of the carcinogens certain prolonged contacts of cells with the substances obtain, in the alimentary canal there is a constant "wash" of materials over the surfaces. Furthermore, these surfaces are covered by a layer of mucus.

SUMMARY

Because of the chemical relationship of methylcholanthrene, one of the most potent carcinogens, to bile acids, which normally bathe a large portion of the gastrointestinal tract, feeding experiments with this substance were carried out on mice.

Of 48 mice observed for periods ranging up to one hundred and eighty-six days, 2 presented benign squamous epithelial papilloma of the fundus of the stomach. One of these also presented a carcinoma of the outer aspect of the right cheek, 1 a carcinoma of the buccal mucosa over the mandible with invasion of the latter, 1 a hypopharyngeal carcinoma, 1 a carcinoma of the angle of the mouth, involving the mucosa and the contiguous skin of the cheek, 1 a squamous cell carcinoma of the skin on the right side of the chin, 1 a benign papilloma of the skin over the right mandible and 1 several small papillomas scattered over the chin.

AVULSION FRACTURE OF THE GREAT TROCHANTER

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Interest in the present study of isolated fracture of the great trochanter was stimulated by a necessity which recently arose for answering questions having medicolegal significance. The need for such a study was appreciated the more when it was realized that, instead of being casual and commonplace, this type of fracture is extremely interesting and unusual.[1] In spite of carrying on a moderately active hospital and private practice involving the treatment of many industrial accidents, I have personally observed only 3 cases during more than fifteen years. A fairly careful search by the attending roentgenologist of the extensive dispensary and inpatient files of the roentgenologic department of the Hospital for Joint Diseases disclosed only 4 additional cases classified under the diagnosis of fracture of the great trochanter. Final recourse to a number of standard textbooks dealing with the subject of fractures [2] was but slightly more gratifying, if at all. One author dismissed the subject without mention. Another described only the epiphysial separation occurring in patients under the age of 18. Others gave descriptions, which, though more extensive and extremely helpful, still did not clearly define the clinical picture in terms which

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From the service of Dr. Harry Finkelstein at the Hospital for Joint Diseases.

Read before the American Academy of Orthopedic Surgeons, Los Angeles, Jan. 20, 1938.

1. (*a*) Eboil, J.: Ann. brasil. de med., Rio de Janeiro **29**:76, 1877. (*b*) Feinen, J.: Deutsche Ztschr. f. Chir. **99**:444, 1909. (*c*) Krüger: ibid. **83**:464, 1906. (*d*) Neugebauer, G.: Med. Klin. **17**:1358, 1921. (*e*) Stein: Deutsche med. Wchnschr. **32**:818, 1906.

2. (*a*) Key, J. A., and Conwell, H. E.: The Management of Fractures, Dislocations and Sprains, St. Louis, C. V. Mosby Company, 1934, p. 780. (*b*) Magnuson, P. B.: Fractures, Philadelphia, J. B. Lippincott Company, 1933. (*c*) Scudder, C. L.: The Treatment of Fractures, with Notes upon a Few Common Dislocations, ed. 10, Philadelphia, W. B. Saunders Company, 1926, p. 530. (*d*) Speed, K.: A Text-Book of Fractures and Dislocations, Philadelphia, Lea & Febiger, 1916, p. 397. (*e*) Stimson, L. A.: A Practical Treatise on Fractures and Dislocations, ed. 8, Philadelphia, Lea & Febiger, 1917, p. 397. (*f*) Wilson, P. D., and Cochrane, W. A.: Fractures and Dislocations, Philadelphia, J. B. Lippincott Company, 1925, p. 515.

fit the cases here studied. Because of this it is felt that presentation of even limited material will be condoned.

While a series of 7 cases would not seem to warrant the didactic setting up of any elaborate system of classification, it will be noted that the cases here reported cannot be discussed together unless it is clearly realized that they fall naturally into three smaller categories. On the basis of the age of the patient, fractures of the great trochanter may be divided into the epiphysial separations of adolescence and the true fractures of adulthood. The former occur in patients under the age of 18, before the closure of the epiphysial line, and involve the whole of the great trochanter. The latter usually do not involve the whole of the trochanter and, on the basis of the etiologic mechanism, may be subdivided into those which are caused by accidental injury and those which are due to muscular violence. In the present series 6 cases of true fracture and 1 of epiphysial separation were found.

REPORT OF CASE OF EPIPHYSIAL SEPARATION

CASE 1.—Rita B., aged 3 years, first appeared in the outpatient service in December 1930, with a flexion contracture of the elbow. There was a history of multiple articular disease following pyemia, for which the patient had been treated in another institution before her admission to the Hospital for Joint Diseases. On Oct. 5, 1935, it is recorded that the patient, then aged 8 years, had fallen while skating and had suffered "complete oblique fracture at the junction of the middle and distal thirds of the shaft of the left tibia, with good alinement of the fragments." A plaster bandage was applied and was left on until Dec. 14, 1935. In February 1936 it was noted that "the child walks with a slight limp on the left side, holding the left foot everted. Examination shows apparently good healing of the line of fracture—no shortening and no tenderness. The foot is somewhat swollen." In October 1936 it was first noted that "the patient complains of pain in both lower limbs, mainly the left one. Examination of the foot gave results essentially negative." A diagnosis of epiphysiolysis was made, and a roentgenogram of the left hip was requested. Though the symptoms did not seem to point to involvement of the right hip, roentgenograms were made of both hips for comparison. This film (fig. 1) was reported by Dr. M. M. Pomeranz to show "a fragmentation of the right greater trochanter, with separation of two small fragments of bone. There is a slight hiatus between the greater trochanter and the shaft of the femur at the epiphysial line. No such hiatus exists in the identical area on the opposite side. Extending from the base of the epiphysis downward in the soft tissues, external to the femoral shaft, for a distance of 3 inches (7.6 cm.), linear calcification is present. The diagnosis is fracture of the epiphysis of the greater trochanter with an ossifying process in the soft tissues of the thigh below."

ETIOLOGY

Apart from the question of diagnosis, the main interest in fracture of the trochanter lies in the discussion of the mechanism of its production. While it is true that in the preceding case there was antecedent trauma, the relationship of the direct injury in the left leg to

the roentgenographic signs inadvertently found in the opposite leg may well be questioned. Moreover, the presence of an earlier infection and the possibility that an unnoticed muscular injury to the right leg may have been suffered at the time of the original accident serve to stimulate a wide difference of opinion as to the ultimate cause, though the fracture is probably to be grouped among the epiphysial separations.

Fig. 1 (case 1).—The calcific shadow is disposed over the whole length of the trochanter and extends into the soft tissues. There is a slight increase in the width of the epiphysial line as compared with that on the opposite side. The fragmented shadow is reminiscent of the picture occasionally seen in periosteal ossification or in peritrochanteric bursitis.

With epiphysial separations occurring as they do during the period of greatest growth, it would seem reasonable to attribute them to trauma or to the avulsing action of the muscles which are inserted into the trochanter. On this question, however, there appears to be

considerable difference of opinion in the literature. Poland [3] stated, ". . . that the injury is almost always the result of direct violence, such as a fall on the hip, or a severe blow on the trochanter." Though he noted the frequency with which infection was associated with epiphysial separation, he did not particularly stress the relationship. Similarly, he mentioned several cases in which muscular pull might have been considered the causative factor, but he specifically deprecated the validity of the supposition as unproved by autopsy. Stimson,[2e] on the other hand, commented: "In all but one (Daniels) the separation was exactly along the epiphysial line and the fragment was not displaced; it seems highly probable that they were cases of osteomyelitis, possibly originating in trauma."

In the more recent writings on this subject,[4] the significance of infection is almost completely neglected in favor of direct blows or indirect muscular violence. Unfortunately, epiphysial separations and forms of fracture which occur in adults are grouped together in these later discussions. Though casual mention is made of the fact that fractures of the trochanter in adults may result from muscular effort, the impression is conveyed that avulsion more commonly occurs in cases of epiphysial separation of adolescence, while direct violence is the more common cause of fracture in adults. Thus Speed, in the most recent edition of his excellent textbook, stated:

> This fracture (of the great trochanter) is infrequent and is caused either by direct violence received on the trochanter, or by muscular action of the external rotators of the thigh attached to the great trochanter, accompanied by torsion of the whole limb inward. In the latter instance, the separation generally follows the old epiphyseal plane, especially when it occurs in adolescence.

With this opinion the experience gained in the present series is only partially in accord. It appears that those epiphysial separations which may be attributed to muscular action can be explained only on the assumption that the gluteal muscles, and not the external rotators, are the disrupting force. On the other hand, it appears that the external rotators result in an avulsion fracture of the tip rather than of the body of the great trochanter. Contrary to the general belief that direct external trauma is the most common cause of these fractures, the cases here recorded lead to the conviction that the larger number are caused by indirect muscular violence. Of the 6 fractures in adults only 1 (case 2) can be unequivocally attributed to a direct blow, while the other 5, due to muscular action, constitute a subgroup as characteristic of the adult as epiphysial separation is of the adolescent.

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3. Poland, J.: Traumatic Separation of the Epiphyses, London, Smith, Elder & Co., 1898, p. 662.

4. (*a*) Kummer, A.: Nederl. tijdschr. v. geneesk. **78**:1324, 1934. (*b*) Key and Conwell.[2a] (*c*) Scudder.[2c] (*d*) Speed.[2d]

REPORT OF CASES OF TRUE FRACTURE IN ADULTS

The case which immediately follows, that of a fracture due to a direct blow, is presented in the barest detail and largely for contrast with the succeeding 5 cases, which illustrate the main theme of this communication—avulsion fractures of the tip of the great trochanter.

Fig. 2 (case 2).—Small chip fracture off the upper portion of the trochanter, due to a severe external blow.

CASE 2.—Robert N., a contractor aged 25, was admitted to the hospital on July 20, 1928. The patient stated that while descending from a trolley car he had been struck and thrown down by a passing automobile truck. He was taken to a municipal hospital, where it is alleged that a dislocation of the left hip was reduced. On admission to the Hospital for Joint Diseases the patient showed abrasions and contusions about the left ilium and walked with difficulty. Roentgen examination "disclosed the hip in marked abduction, with a chip off the greater trochanter at its upper and anterior margin" (fig. 2). No statement of the treatment was made. Six days after admission the patient was discharged. In

October 1930 he again visited his physician, this time with a complaint of pain, especially on change of weather. Examination at this time elicited no objective evidence of any disability attributable to the earlier injury.

CASE 3.—Bertha L., a housewife aged 70, was admitted to the hospital on Nov. 12, 1932. She had fallen on her left side and afterward had been unable to get up or to walk. She had been brought to the hospital in an ambulance.

Examination disclosed no shortening of the limb. The distance from the anterior superior spine of the ilium to the internal malleolus of the tibia measured for the

Fig. 3 (case 3).—Typical avulsion fracture of the great trochanter at its posterosuperior angle. The line of fracture is approximately at the level of the junction of the trochanter and the neck. The leg is in slight external rotation.

right leg 30⅜ inches (77.2 cm.) and for the left 30¼ inches (76.8 cm.). The left limb was held in 5 degree adduction and in 10 degree external rotation. Adduction was possible to 20 degrees and flexion to 90 degrees, with pain. A roentgenogram (fig. 3) "disclosed a complete fracture through the greater trochanter, with upward and inward displacement of the fractured fragment." Traction was applied to the limb. On Nov. 29, 1932, the patient was discharged. No subsequent data on this case could be obtained.

Case 4.—Thomas M., aged 48, was seen in the outpatient department on March 19, 1934, with a history of having fallen and "struck the stump of his amputated left leg some twelve days before. He had pain and tenderness in the region of the trochanter." Later, "considerable local induration of the great trochanter was noted." The roentgenogram was reported by Dr. Pomeranz as showing "complete oblique fracture of the greater trochanter. The line of fracture begins at the inner aspect of the base of this prominence and extends obliquely upward and outward to the cortex ½ inch (1.3 cm.) below its upper limit. At the latter site two small spicules of bone are noted. There is no separation of the fragments." (The line of fracture was almost identical with that seen in the other similar cases; a reproduction was not prepared because the line was just barely discernible on the original roentgenographic plate.) Physical therapy was prescribed, with the understanding that if there was no improvement a plaster of paris spica was to be applied. In the absence of any contrary note in the record, the inference may be drawn that there was no need for any modification of the treatment employed. The patient later disappeared from observation.

Case 5.—Harry La C., a janitor aged 47, fell off a ladder while at work on Sept. 10, 1934. The patient complained of moderate pain over the great trochanter and of limitation of motion in the hip. There was tenderness on pressure over the trochanter but no evidence of ecchymosis or of injury to the overlying soft tissues. Both legs were of equal length. Roentgen examination was advised but was not made until a week later at the urgent insistence of the attending physician. The film was reported as showing "a recent fracture through the left great trochanter at its upper pole. The fragments are in good position." At this time immobilization in a plaster of paris spica was advised. The patient refused to submit to this treatment and continued with his work as house superintendent. Except for physical therapy, no treatment was given. Complete recovery, without any disability, was subsequently reported.

Case 6.—George T., a writer aged 37, was seen on May 28, 1935, the day after his injury. The patient stated that he had fallen from a ladder, landing on his right side and striking his hip. He could not recall all the details, but he believed that while attempting to protect himself in his fall he had "strained his right hip and felt something give way." Though complaining of pain, he was able to rise, to bear weight and to walk into his house with some assistance. He noted that he walked awkwardly and that the right leg seemed suddenly longer than the left. Examination disclosed slight ecchymosis about the great trochanter. There was tenderness in this area on pressure, and the motion of the hip in all directions was limited by pain. The leg was held in slight external rotation, and the tip of the trochanter appeared to be above Nélaton's line. A tentative diagnosis of impacted fracture of the femoral neck was ventured, despite the fact that measurement of the distance between the anterior superior spine of the ilium and the internal malleolus revealed no variation in length between the injured leg and the normal leg. The significance of this apparent paradox was not realized until the roentgenogram (fig. 4) disclosed that the patient had suffered an avulsion fracture of the tip of the great trochanter.

Because of the pain, the leg was immobilized in a plaster of paris spica in the position of abduction and slight external rotation for about eight weeks. On removal of the spica, union was found to be solid, and the patient was able actively to abduct and externally to rotate the leg. After a short period of physical therapy to overcome the stiffness the patient made a complete recovery.

CASE 7.—Opinion in the case of David G., a laborer aged 28, was requested on March 11, 1937, with particular reference to the necessity or advisability of open operation in the treatment of a fracture of the tip of the great trochanter. The patient alleged that while fixing a boiler he had fallen a distance of 3 or 4 feet (38 to 41 cm.) and had landed on a pile of bricks, striking his right hip. He complained of severe pain and inability to walk. He was taken to a nearby hospital, where a roentgenogram showed a fracture of the tip of the great trochanter (fig. 5). The physician in charge suggested immediate operation.

Fig. 4 (case 6).—Typical fracture resembling that in figure 3.

When examined several days after his injury, the patient was found to have no external signs of contusion or abrasion of the skin. There were moderate tenderness on pressure over the trochanter and slight limitation of motion by pain. There was no shortening of the affected leg. Immobilization in a plaster of paris spica with the leg in abduction was recommended. Because of the lack of cooperation on the part of the patient and the subsidence of symptoms, even this measure was not undertaken by the attending physician. Rest in bed was advised but was never carried out. During his waking hours the patient seldom

rested and was frequently out of bed. Nevertheless, recovery was apparently uneventful, and at the end of about three weeks the patient was discharged from the hospital. Some two months later the opportunity for examining this patient in court presented itself. The patient claimed inability to use the leg normally, but careful examination disclosed no limitation of motion, either active or passive.

COMMENT

Several features of this type of fracture stand out significantly. Though there is invariably a history of a fall, it is interesting to note

Fig. 5 (case 7).—Typical fracture resembling that in figure 3.

that there is almost never any evidence of injury to the overlying soft tissues and seldom even any signs of ecchymosis. Moreover, the fact that neither the distance fallen nor the weight of the falling body nor the angle or manner of impact materially modifies the resulting bony lesion is remarkable and seems to suggest the operation of a factor other than external force. This possibility is further emphasized by the roentgenographic appearance of the fracture. Roentgenographically these fractures resemble one another, so that the roentgenogram of any one might, with but slight concessions, be mistaken for that of any of

the others. The area involved is always that portion of the trochanter which projects upward and backward from its line of junction with the neck of the femur. The size of the fragment and even the direction of the line of fracture are, with minor variations, almost identical. There is usually no comminution of the fragment and no depression of the cortex at the site of the alleged impact.

Though most authors have expressed adherence to the belief that these fractures are due to external violence, there is but little autoptic or experimental data on which to base an accurate opinion of the pathology of the condition.[5] It seems extremely unlikely, on the law of averages, that such an invariable clinical picture should be the effect of haphazard unpredictable accident. The appearance of the fracture is so unvarying that it can be conceived of only as the outcome of an etiologic mechanism in which both the force and the point of application are relatively constant. These characteristics accurately define an internal avulsing rather than an external contusing causative agent. Neugebauer [1d] reported a case in which the patient fell on one side and suffered the typical fracture on the opposite side. At first thought it might appear that the action of the powerful gluteal muscles would be the competent producing cause of the fracture. That this may be true of the epiphysial separations of adolescence is indicated by the dissections which Poland reported. On the other hand, the inadequacy of this explanation—indeed its impossibility—in respect to the adult type of fracture is revealed by a closer scrutiny of trochanteric anatomy.

The trochanter is described in general as a quadrilateral prominence at the upper end of the femur, at the junction of the neck and the upper part of the shaft.[6] In adults, the epiphysial line is closed, and the greater part of the trochanter has become so closely united with the femur that there is no line of demarcation between shaft, neck and trochanter, except at the upper pole of the last. In its anterior portion the projection of the trochanter above the level of the neck is minimal. Its posterior half, however, projects considerably above and behind the planes of the femoral neck. This constitutes the posterosuperior angle, triangular and bounded below by the line of fusion with the neck and above and behind by the superior and posterior borders of the trochanter. To the medial surface of this portion of the bone, the external rotators of the thigh, the internal and external obturators, the superior and inferior gemelli and the pyriformis muscle are attached.

5. Ashton, J. H.: Lancet **1**:231, 1875. Clarke, J.: Tr. M. & Phys. Soc. Calcutta **7**:398, 1835. Waechter: Deutsche Ztschr. f. Chir. **8**:104, 1877. Warren, F. W.: Dublin J. M. Sc. **62**:69, 1876.

6. Gray, H.: Anatomy of the Human Body, ed. 22, revised by W. H. Lewis, Philadelphia, Lea & Febiger, 1930.

> The lateral surface, quadrilateral in form, is broad, rough, convex and marked by a diagonal impression which extends from the posterosuperior to the anteroinferior angle and which serves for the attachment of the gluteus medius muscle . . .[6a]

In the triangular area above and in front of this diagonal, the gluteus minimus is inserted, while the gluteus maximus is partly attached behind and below at the base of the posteroinferior portion of the trochanter (fig. 6).

Judging from its insertion alone, the action of the gluteus minimus should be the avulsion of the anterosuperior angle; the action of the gluteus maximus should be the tearing away of a portion of the posteroinferior angle, while the gluteus medius, acting either alone or in conjunction with the other gluteal muscles, should tend to avulse the whole trochanter. Since none of these areas is involved in the typical adult fracture, it is apparent that the groups of muscles mentioned cannot be implicated when the responsibility for the condition is assigned.

There remains, then, only the group of the external rotator muscles. Since these are attached to the medial aspect of the posterosuperior angle of the great trochanter, their unopposed action alone can explain the constancy of the fracture line and the tendency of the fragment to be drawn upward, backward and inward in the direction of contraction of the muscle fibers. That this displacement is slight is in all likelihood due to the insertion of the gluteus medius "into the oblique ridge which runs downward and forward on the lateral surface of the greater trochanter."[6b] This line is at right angles to the line of fracture. The consequence is that the insertion of the gluteus medius straddles the fracture line and by its contraction tends to counteract rather than to participate in the displacement of the fragment. It is only when the injury has been sufficient to tear the tendon to the gluteus medius that major separations of the free fragment occur.

Though this interpretation appears to offer a ready explanation of the facts, it has not been accepted by many observers. In the German literature there is talk of an "Abriszfraktur," that is, an avulsion fracture, yet some German authors in their texts have categorically stated that this fracture can occur only as the result of a direct blow. In the French literature, too, Broca is said to have admitted the possibility of avulsion fracture without ever having seen one. The very knowledge that competent observers have expressed doubt as to the importance of muscular action alone suggests the possibility that other factors, such as trauma, may be contributory elements in the mechanism of production. It may be that the fall so frequently associated with this type of fracture establishes a line of cleavage in a crystalline structure that is already

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6a. Gray,[6] p. 240.

6b. Gray,[6] p. 473.

stressed by powerful muscular forces. On the other hand, the relationship may be entirely coincidental. Whatever the connection, there can be no doubt that only on the basis of the primary muscular pull can the distinguishing features of this fracture be readily explained and the clinical picture rationally synthesized.

CLINICAL DIAGNOSIS

Apart from the general symptoms—the history of a fall, the difficulty in walking though weight bearing is possible, the tenderness on

Fig. 6.—Side view of the great trochanter. The oblique line along which the gluteus medius muscle is inserted is shaded light and runs downward and forward from the posterosuperior angle to the anteroinferior angle. The triangular posterosuperior angle is shaded dark and presents only its lateral aspect. On the medial aspect, not shown in the photograph, the external rotator muscles of the thigh are inserted.

pressure over the trochanter, and the pain and limitation of motion in the hip—there are certain data which have been considered of especial importance in the establishment of a clinical diagnosis. In cases of epiphysial separation Kummer [4a] described a shuffling gait, with the hip held in abduction and extension, which he stated was typical. Indeed, he particularly stressed the attitude of extension as a sign of

capital importance in differentiating an epiphysial separation from acute coxitis, which, especially in the early phases, it may closely resemble. On the other hand, Thienhaus [7] reproduced a photograph which indicated that in his opinion adduction and internal rotation of the thigh, with flexion of the hip and the knee, are characteristic. After fracture in the adult Betto [8] and Jáki [9] have expressed agreement with Thienhaus that internal rotation and adduction is the position assumed. In this series the attitude was not specifically commented on, though in 2 cases it was recorded that the leg lay in external rotation. Downward tilting of the pelvis on the affected side has been noted by both Betto and Kummer. This position is doubtless of reflex origin and probably results from the necessity for relaxing the spastic muscles in the injured area. Kummer stressed it as the explanation of the apparent lengthening, which several authors have reported in this condition. Betto called attention to the fact that the patient resists passive internal rotation and cannot produce active external rotation. Theoretically, this selective limitation of motion should be a diagnostic aid of some importance. Practically, its value is extremely problematic, since in the acute stage all motions at the hip are interdicted by pain.

Still another sign, which was noted but improperly evaluated, warrants special mention. In case 6 it has been recorded that the trochanter appeared to be above Nélaton's line and that the length of extremities measured from the anterior superior iliac spine to the internal malleolus of the ankle was the same. Normally the tip of the trochanter lies on a line which connects the anterosuperior spine of the ilium with the most prominent point of the ischial tuberosity. In casual daily practice the elevation of the tip of the trochanter above this line, or the shortening of the base of Bryant's triangle, has been taken to imply an associated shortening of the limb, which could be due to any of a number of conditions focused at some point between the iliac spine and the base of the great trochanter. A little reflection, however, will quickly lead to the conviction that this assumption is not necessarily true under either of two sets of circumstances. In the first place, a normal trochanter may appear to be above Nélaton's line if the end points of the line are lower than normal. This may occur, for example, when there has been a fracture or an avulsion of the iliac spine or of the ischial tuberosity, and it need not detain me beyond mere mention. In the second place, the trochanter may appear to be above Nélaton's line if the trochanter itself is the seat of the lesion, even though the position of the line is normal.

7. Thienhaus, C. O.: Ann. Surg. **43**:753, 1906.

8. Betto, O.: Chir. d. org. di movimento **22**:58, 1936.

9. Jáki, J.: Zentralbl. f. Chir. **63**:1169, 1936.

It is apparent, then, that the statement of the position of the tip of the trochanter acquires meaning only when there is a specific statement as to the position of the line in relation to which the trochanter appears elevated. The correct evaluation of the relationship, therefore, involves a careful comparative measurement of the distance from the internal malleolus to the iliac spine and to the ischial tuberosity on both sides. If either of these lengths is less on the affected side than on the normal side and the trochanter is elevated, any one of a number of conditions may be encountered. If the lengths of the limbs are unchanged, however, and the trochanter is elevated, the tip of the trochanter alone must be abnormal.[10] In the presence of tenderness over the trochanter following an alleged injury, the conjunction of signs mentioned indicates an epiphysial separation in an adolescent or a fracture of the trochanter in an adult. When it is present, this sign is pathognomonic. Unfortunately, it is often not elicited (1) because the exquisite trochanteric tenderness precludes accurate palpation of the tip and (2) because the separation of the fragments is often so slight as to be immeasurable under the skin. When the separation is measurable the relative increase in the distance between the tip of the trochanter and the tip of the external malleolus is pathognomonic.

DIFFERENTIAL DIAGNOSIS

In cases in which the aforementioned special signs cannot be elicited, the differential diagnosis is to be made on a careful interpretation of the clinical data and, in the last analysis, on the roentgenographic appearance. The commoner conditions which may simulate fracture of the great trochanter, such as fracture of the neck of the femur, dislocation of its head and inflammatory diseases like coxitis or peritrochanteric bursitis, can usually be readily differentiated. Occasionally, however, one encounters a case like those following, in which even the roentgenogram, if hastily examined, may give rise to an erroneous impression.

CASE 8.—Felix L., a laborer aged 30, was first seen in the outpatient department after a fall and an alleged injury to the left hip and knee. The patient complained of no disability, continued at his work and came for treatment of abrasions about the knee. It was only after several days that he began to complain of gradually increasing pain and progressive limitation of motion at the hip. Examination disclosed marked tenderness on pressure over the trochanter but no sign of external injury. All motions of the hip caused pain. There was no difference in the measurements of the legs, and the relationship of the trochanter to Nélaton's line was not noted. A tentative diagnosis of fracture of the great trochanter was made and a roentgenogram ordered (fig. 7). A casual view appeared to confirm the clinical impression, because of the presence of the triangular shadow constantly seen in cases of avulsion fracture. A more careful examination of the

10. Milch, H.: M. Rec. **147**:229, 1938.

film disclosed that the trochanter was normal in outline but was surmounted by a second triangular shadow, which was reported as indicating "irregular calcific deposits adjacent to and above the great trochanter, owing to calcification in the gluteus tendon." The patient was subsequently aspirated, and the recovery of the chalky material typical of peritrochanteric, or so-called calcific gluteal, bursitis confirmed the roentgen diagnosis.

CASE 9.—S. P., aged 40, was seen in the outpatient department in January 1928, when he presented himself for symptoms suggesting pain in the lower part

Fig. 7 (case 8).—The faint cockade-shaped shadow lying directly above the tip of the great trochanter is due to a chalky deposit in the gluteus medius muscle. The case was one of peritrochanteric or calcified gluteal bursitis. The normal posterosuperior angle of the trochanter is seen directly below.

of the back. In the course of a routine examination, a roentgenogram disclosed what appeared to be an old avulsion fracture of the left great trochanter (fig.8). Although the patient was not complaining of symptoms in the left hip, it was thought that some slight restriction of motion was present.

An effort at obtaining the history of this injury from the hospital at which he had been treated previously revealed that about a year before the patient had been thrown off the back of a truck and apparently had suffered a cerebral

injury, as well as an injury to his left hip. He was given emergency treatment at one of the city hospitals. After four or five days he was discharged to the care of his private physician, who instituted no specific treatment for the injury to the left hip. About six days later he was admitted to the hospital because of pain in the left hip, and at this time a roentgenogram revealed an "old fracture of the great trochanter, with upward and inward displacement of the smaller fragments." The Wassermann reaction was reported as 4 plus. A splint was applied, and the patient was discharged after about three weeks. He apparently received no further treatment.

Fig. 8 (case 9).—Old avulsion fracture of the great trochanter, with moderate displacement and solid union.

TREATMENT

In the matter of treatment little need be said. Healing almost invariably takes place. This is attested by the uncomplicated outcome of numerous operative procedures which involve preliminary cutting of the trochanter. Because the fibers of the gluteus medius prevent excessive separation of the fragments, the patients usually require little more than temporary immobilization with a plaster of paris bandage. To overcome the tension on the avulsing muscles the spica should be applied

with the extremity in abduction, extension and slight external rotation. This is the orthodox treatment. Neglect to immobilize would certainly subject the surgeon to unpleasantness in the event that any inadvertent motion led to excessive separation of the fragments. On the other hand, the evidence afforded by several of the cases reported would indicate that perfectly adequate healing, without any residual disability, may occur even in the absence of any immobilization. Under these circumstances, it is obvious that the question of operative intervention need not arise in the average case. At worst, the indication for surgical suture of the fracture may present itself only in cases of wide separation of the fragments, in which nonunion or muscular atrophy is feared.

SUMMARY AND CONCLUSION

A series of 8 cases of the relatively unusual, isolated fracture of the great trochanter is presented. These cases may be divided into those of epiphysial separation and those of avulsion. Six of the cases of the present series must be classified as instances of avulsion fracture resulting from excessive pull of the external rotator muscles of the thigh. The symptoms are discussed. Elevation of the trochanter in the absence of any change in length of the leg is pathognomonic of the condition. Immobilization is the treatment of choice, even though satisfactory results have been obtained even in cases in which expectant treatment was used. Only in cases in which wide separation of the fragments has occurred are open operation and suture of bone indicated.

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INTESTINAL OBSTRUCTION DUE TO GALLSTONES

REPORT OF TEN CASES

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Intestinal obstruction due to gallstones is a relatively rare condition. In 1890, Courvoisier [1] reported 131 cases, and in 1917 Wagner [2] found reports of 333 cases in the literature. Since that time numerous isolated instances and small series have been reported. During the past ten years, 10 cases have been observed at the University Hospital, constituting 5.3 per cent of all cases of intestinal obstruction.

A large gallstone may enter the lumen of the gastrointestinal tract through the common bile duct or through a fistula between the gallbladder and the bowel. The latter route is the more common. Such fistulas form at the site of inflammatory adherence of an adjacent viscus, usually the duodenum, to the gallbladder. Associated pressure of the gallstone causes necrosis and erosion of the gallbladder and the intestinal walls. Expulsion of the stone into the gastrointestinal tract may occur at the time of formation of the fistula or at any time subsequently.

A correct preoperative diagnosis of this condition is frequently impossible. The symptomatic history of many patients does not point directly to disease of the biliary tract. Furthermore, if the patient has had previously recognized disease of the gallbladder, the early symptoms of obstruction are easily misinterpreted since the pain, nausea and vomiting resulting from obstruction are not unlike the symptoms produced by an acute biliary attack.

Early examination reveals little except tenderness in the upper part of the abdomen. Abdominal distention is rarely noted early, and because most patients with this condition are obese it may not be noted until late in the course of the difficulty. The obstruction may or may not be complete and may be persistent or intermittent.

A plain teleroentgenogram of the abdomen will occasionally visualize the stone. Often, dilated loops of small bowel with many fluid

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1. Courvoisier, L. G.: Casuistisch-statistische Beiträge zur Pathologie und Chirurgie der Gallenwege, Leipzig, F. C. W. Vogel, 1890, p. 101.

2. Wagner, A.: Ileus durch Gallensteine, Deutsche Ztschr. f. Chir. **130**:353, 1914.

levels are apparent on the film, so that a diagnosis of obstruction in the small bowel is made.

A reduction of the mortality from this condition can be accomplished only by early diagnosis and operation. In some instances at operation the stone may be crushed within the lumen of the bowel or "milked" distally into the large bowel, but care must be taken that the bowel wall is not injured by the manipulation.

REPORT OF CASES

CASE 1.—Mrs. E. C., aged 49, was admitted to the University Hospital on March 5, 1936, because of cramping abdominal pains and intermittent vomiting during the past eight days. Eight months prior to her present admission a total abdominal hysterectomy and bilateral salpingo-oophorectomy for a carcinoma of the body of the uterus had been performed, followed by an intensive course of irradiation therapy. Except for the carcinoma she had always been in good health until eight days before the present admission, when she noticed a dull pain in the right upper quadrant of the abdomen, with subsequent vomiting and increasing constipation.

Physical examination showed an obese white woman who was acutely ill and moderately dehydrated. Abdominal examination revealed some distention and generalized tenderness. Urinalysis and laboratory examination of the blood, including determination of the blood chlorides, the carbon dioxide–combining power and the urea nitrogen content, all gave normal results.

A diagnosis of intestinal obstruction secondary to neoplastic invasion was made, and conservative treatment was given. On the eleventh day of hospitalization, after the diet had been gradually increased, the symptoms recurred, and an emergency operation was performed. A gallstone 4.5 by 3.5 by 3.5 cm. was found in the ileum. Proximal and distal to this point the bowel was thickened and dilated. In an attempt to explain the dilation and thickening of the bowel distal to the obstruction, a second stone, slightly smaller than the first, was found 15 cm. from the ileocecal valve. The second stone was 70 cm. from the first. Both stones were removed through a single incision in the bowel wall. Palpation of the gallbladder revealed this organ to be adherent to the duodenum. The postoperative course was satisfactory.

Comment.—This case is of interest because of the absence of symptoms suggestive of disease of the biliary tract prior to the present illness and because two stones were present within the small bowel, each causing an independent point of obstruction.

CASE 2.—Mrs. L. S., aged 52, was admitted to the University Hospital on Jan. 24, 1933, because of abdominal pains and vomiting of five weeks' duration. The present illness had started with severe pain in the right upper quadrant of the abdomen. The pain radiated to beneath the right scapula and was diagnosed by her physician as gallbladder colic. She was confined to bed most of the time because of repeated attacks of similar trouble. One week prior to admission there had been severe episodes of vomiting. A recent diagnosis of diabetes mellitus had also been made.

Physical examination revealed an obese, apathetic, irritable, acutely ill woman. The heart sounds were faint; the blood pressure was 110 systolic and 85 diastolic. Distention, generalized rigidity and acute tenderness were present in the mid-abdominal region. On auscultation the abdomen was "quiet."

The erythrocyte count was 5,250,000, the hemoglobin 110 per cent and the leukocyte count 10,200. Examination of the urine showed glycosuria. Determination of the sugar content of the blood revealed 375 mg. per hundred cubic centimeters. The carbon dioxide–combining power of the blood plasma was 44.7 per cent. A diagnosis was made of diabetes mellitus with possibly an acute abdominal condition of undetermined character.

Treatment of the diabetes was instituted, and the patient's condition was improving until the morning of the third day of hospitalization, when she suddenly had severe abdominal pain with increasing symptoms and signs of shock. She died within an hour.

Postmortem examination revealed an obstruction of the small intestine, caused by a gallstone measuring 4.5 by 2.8 by 2.5 cm., which was lodged 20 cm. from the ileocecal valve. There was a recent perforation on the antimesenteric side of the bowel, 15 cm. above the stone. Moderately acute cholecystitis and a cholecystoduodenal fistula 2.5 cm. in diameter were present.

Comment.—This case demonstrates the ease with which severe diabetes may mask an acute intra-abdominal catastrophe and influence treatment.

CASE 3.—Mrs. R. W., aged 72, was admitted to the University Hospital on June 3, 1936, because of generalized abdominal pain, vomiting and obstipation of four days' duration. She had always had good health except for a single attack of gallbladder colic eight years before the present admission.

Physical examination disclosed an obese, dehydrated, acutely ill white woman. The lungs were clear. The heart was somewhat enlarged, with an auricular fibrillation. The blood pressure was 120 systolic and 70 diastolic. There was moderate abdominal distention, with tenderness in the upper part of the abdomen and borborygmus about the umbilicus.

Routine laboratory examinations gave normal results. A teleroentgenogram showed dilated loops of small bowel with fluid levels.

A diagnosis of intestinal obstruction was made, but because of the precarious condition of the patient operation was deferred, and parenteral administration of fluids, continuous gastric suction and enemas were given. Four hours later pulmonary edema suddenly developed, and she died after atropine, venesection and cardiac stimulants had failed to give relief.

At postmortem examination a gallstone 7 by 5 by 5 cm. was observed in the ileum 7 cm. from the ileocecal valve. It had caused complete obstruction. Additional significant findings included a cholecystoduodenal fistula 2 cm. in diameter, pulmonary edema, chronic myocardial degeneration and generalized arteriosclerosis.

Comment.—Except for the single attack eight years previously, there was nothing in the history to suggest the cause of the obstruction.

CASE 4.—Mrs. R. P., aged 30, was admitted to the University Hospital on Aug. 21, 1932, complaining of the classic symptoms of obstruction of the small bowel, which had occurred intermittently for the past eight days, with occasional relief after repeated enemas.

On examination she cooperated poorly, being toxic and acutely ill. There were abdominal distention, diffuse tenderness and borborygmus over the entire abdomen. The routine laboratory examination gave essentially normal results. A plain flap teleroentgenogram revealed the classic picture of obstruction of the small bowel.

With conservative management she made definite improvement for forty-eight hours; then the symptoms increased. An emergency operation was done. A gallstone 5 by 3 by 3 cm. was lodged in the ileum, 10 cm. from the ileocecal valve. It could be easily crushed within the lumen of the bowel and the fragments pushed into the cecum. The gallbladder was adherent to the duodenum and the stomach. Postoperatively her condition became more critical, and she died twenty-four hours later.

Comment.—Because this patient had no history of disease of the biliary tract and was only 30 years old the correct cause of the obstruction was not considered before operation.

CASE 5.—Mrs. C. S., aged 83, was known to have diabetes. She was admitted to the University Hospital on Jan. 21, 1935, complaining of severe, generalized abdominal pains. During the past four years she had had repeated attacks of pain in the right upper quadrant of the abodmen. The attacks had been occurring with increasing frequency and severity, and two days before the present admission after an episode of colic, the pain was localized in the left side of the abdomen and was associated with large emeses. Her physician reported palpating the gallstones the night before her admission; however, the next morning they had disappeared.

Examination showed a thin woman with pinched facies. There were abdominal distention, generalized tenderness and an intestinal pattern. Laboratory examination of the urine and the blood gave normal results except for a leukocyte count of 22,600.

A diagnosis of intestinal obstruction due to a gallstone was made, and at operation a stone measuring 4 by 2 by 2 cm. was found in the midjejunum. It was impossible to crush the stone within the lumen of the bowel. A short incision was therefore made in the wall of the bowel, and the stone was removed. The postoperative course was satisfactory.

Comment.—The unusual feature of the case was the palpation of the stones in the region of the gallbladder prior to the onset of the obstructive symptoms and their disappearance after the onset. It is significant that age is less a factor in mortality than is an early diagnosis.

CASE 6.—Mrs. A. G., aged 67, was admitted to the University Hospital May 12, 1934. For the past three years the patient had had several typical attacks of gallbladder colic. A severe episode had occurred one year prior to her admission to the hospital. Ten days before admission she had recurring attacks of generalized abdominal pain associated with vomiting.

Abdominal examination revealed distention, moderate tenderness and borborygmus in the left upper quadrant. Laboratory examination of the urine and the blood gave normal results. A teleroentgenogram revealed dilated loops of small bowel, with fluid levels and a negative shadow in the right lower quadrant, which was interpreted as representing a gallstone.

After an adequate amount of parenteral fluids had been administered, operation disclosed a gallstone 3 by 2.5 by 2.5 cm. It was situated 14 cm. from the ileocecal valve. An attempt was made to crush the stone within the lumen of the bowel,

but this failed and resulted in sufficient trauma to necessitate creation of an anastomosis between the ileum and the cecum after removal of the stone. On exploration of the right upper abdominal quadrant the fundus of the gallbladder was found to be adherent to the duodenum. Postoperatively a fecal fistula developed, which subsequently closed.

Comment.—An attempt at milking the stone into the colon is justified, but severe injury to the bowel may result.

CASE 7.—Mrs. A. S., aged 50, was admitted to the University Hospital on April 11, 1927, becaues of abdominal pains and vomiting of four days' duration. A diagnosis of diabetes mellitus had been made one year prior to this admission. During the past eleven years she had frequently suffered from a burning sensation in the epigastrium, at times associated with vomiting. With the recent trouble she also complained of obstipation, although occasionally she would pass a small amount of flatus.

The patient was obese, dehydrated and acutely ill. The abdomen was distended, and generalized tenderness was present, especially marked in the right upper quadrant, where a questionable mass was palpable. Examination of the urine revealed glycosuria. The sugar content of the blood was 325 mg. per hundred cubic centimeters. Examination of the blood otherwise gave normal results except for a leukocyte count of 22,000.

A diagnosis of acute cholecystitis was made, and conservative treatment was administered for four days. Because of increasing symptoms and abnormal findings the diagnosis was changed to acute pancreatitis or intestinal obstruction, and exploration was advised.

At operation a gallstone 5.5 by 4 by 4 cm. was found in the second portion of the duodenum. The stone was removed by incision of the bowel, after which a ligature was placed about the pylorus and a posterior gastrojejunostomy performed in the hope of preventing leakage through the duodenal suture line. The patient's death thirty-six hours after the operation was observed at postmortem examination to have been caused by peritonitis resulting from leakage through the duodenal suture.

Comment.—Although the known tendency of duodenal wounds to leak was anticipated and additional surgical procedures were done, this did not prevent a fatal complication.

CASE 8.—Mr. J. S., aged 56, was admitted to the University Hospital on Oct. 2, 1935, because of gastric trouble of five months' duration. During the past two weeks, one-half hour after each meal he had noticed a dull, aching pain and a feeling of fulness in the epigastrium, associated with episodes of vomiting. The vomitus often contained food eaten the preceding day. He had lost 40 pounds (18.1 Kg.) in weight and much strength since the onset of the trouble.

The patient showed evidence of loss of weight and of protracted illness. The abdomen was flat, with moderate tenderness and rigidity in the epigastrium. Laboratory examinations of the urine and the blood gave normal results. Gastric analysis showed seven points of free hydrochloric acid to be present. Teleroentgenographic studies of the gastrointestinal tract revealed a dilated stomach with almost complete obstruction at the pylorus.

A modified Sippy ulcer regimen for thirteen days failed to improve the patient's condition, and a diagnosis of carcinoma of the stomach having been made, laparotomy was performed. In the pyloric region a hard mass 5 cm. in diameter was found. It was tightly adherent to the under surface of the liver, with apparent invasion

about the gallbladder. The mass was smooth, white and so hard that the surgeon felt it was too firm to be a malignant tumor. There was no evidence of metastasis. Material for biopsy was taken from the mass involving the liver, and a posterior gastrojejunostomy was performed. The patient gradually lost ground and died forty-one days later.

Postmortem examination revealed a pericholecystic abscess secondary to a perforation of the fundus of the gallbladder, with a fistula 2 cm. in diameter between the abscess cavity and the first portion of the duodenum. There were gallstones within the gallbladder, within the abscess cavity and directly opposite the fistula, in the lumen of the duodenum. The gallstone in the duodenum was 2.5 cm. in diameter and completely obstructed the lumen of the bowel. Surrounding the area there was an extensive chronic inflammatory reaction without gross or microscopic evidence of malignancy.

Comment.—This case is of particular interest because preoperatively and at operation a diagnosis of malignant tumor of the stomach seemed logical.

Case 9.—Mrs. A. T., aged 37, was admitted to the University Hospital on Feb. 12, 1936, complaining of recurrent attacks of epigastric pain. In 1925 a cholecystectomy had been performed, the gallbladder having contained numerous small stones and the common duct having shown nothing remarkable. After the cholecystectomy she felt well until one year before the present admission, when she noticed gnawing epigastric distress, aggravated by ingestion of fatty and fried foods and accompanied by much flatulence. She had had fifteen severe attacks of typical gallstone colic, each associated with jaundice, dark urine and clay-colored stools.

The patient on admission did not appear ill, and there was no clinical evidence of jaundice. The abdominal wall was relaxed; there was no muscle spasm and only moderate tenderness to deep palpation in the epigastrium. Laboratory examination of the urine and the blood, including a van den Bergh test, gave normal results.

The day after admission she had a severe attack of colicky epigastric pain accompanied by vomiting, which lasted four hours. A diagnosis of stone of the common duct was made, and she was treated conservatively for six days, with complete relief.

At exploratory laparotomy a round, thin-walled diverticulum measuring 5 cm. in diameter was found. It communicated with the second portion of the duodenum through an opening 2 cm. in diameter just proximal to the ampulla of Vater. The common duct was opened, and no stone or other demonstrable pathologic condition was encountered. Because of the position of the diverticulum in the angle formed by the common duct and the duodenum it was felt this might account for the patient's symptoms of recurrent obstruction of the common duct. The diverticulum was excised and the opening in the duodenum closed.

Postoperatively the patient had an unusual amount of abdominal distention and vomiting, obtaining partial relief by continuous gastric suction. On the sixth postoperative day a duodenal fistula was demonstrated. She continued to vomit intermittently, gradually losing ground and dying on the twenty-fourth postoperative day.

Postmortem examination revealed a fusiform gallstone 6 by 4 by 3 cm. lodged in the small bowel, 23 cm. from the ileocecal valve. It was apparently capable of acting in a ball valve fashion in producing obstruction. The duodenal fistula was well walled off.

Comment.—Explanation of the origin of such a stone in the intestinal lumen is difficult. Large gallstones have been known to be extruded from the common duct. Perhaps in this instance the stone may have been lodged in the duodenal diverticulum and at operation may have been extruded into the duodenum.

CASE 10.—Mrs. N. S., aged 59, was admitted to the University Hospital in June 1937, because of severe, intermittent, crampy abdominal pains associated with vomiting of eight days' duration. There was an increasing degree of obstipation, although she had passed some flatus with each daily enema. During the past ten years she had had typical attacks of gallstone colic, and the onset of the present illness was similar to that of the previous episodes.

The abdomen was somewhat distended, with tenderness throughout, especially over the region of the gallbladder. Urinalysis and examinations of the blood all gave normal results.

A diagnosis of subacute intestinal obstruction probably due to a gallstone was made. At operation a globular gallstone 2 cm. in diameter was found 90 cm. from the ileocecal valve, causing obstruction of the lumen of the bowel. The stone could not be crushed or displaced and was removed after the bowel wall had been opened. Palpation of the gallbladder revealed this organ to be adherent to the duodenum. The postoperative course was satisfactory except for a wound infection which delayed her discharge until the thirty-sixth day.

GENERAL COMMENT

In our experience, intestinal obstruction due to gallstones occurs with sufficient frequency to make it an important consideration in the diagnosis of acute abdominal conditions. This is particularly true when the patient has had previous typical gallstone attacks, but this type of obstruction may occur in a patient who has never had such an attack. Clinical diagnosis is likely to be difficult. The factors which make it so are the similarity of the symptoms to those of an acute gallstone attack and the lack of early physical or laboratory findings which would positively indicate the nature of the condition. In our series only 3 such diagnoses were made preoperatively. In 1 case a diagnosis depended on the disappearance of previously palpable stones in the gallbladder; in another a stone produced a negative filling defect in a flat teleroentgenogram. The diagnosis was made in only 1 case which presented the classic history of previous biliary colic followed by a sudden development of symptoms of acute intestinal obstruction.

We believe that greater alertness in making this diagnosis and more frequent use of the teleroentgenogram will aid in making not only more frequent preoperative diagnoses but earlier diagnoses. While the teleroentgenogram may show only evidences of fluid levels within a dilated bowel, this finding is uncommon except in association with paralytic ileus or mechanical obstruction. In our series, diabetes mellitus was present in 3 of the 10 cases. In 2 instances the diabetes was severe. In no instance, however, was it shown to contribute in any way to the picture produced by the obstructing gallstone.

CONSEQUENCES OF INSTRUMENTAL DILATION OF THE PAPILLA OF VATER

AN EXPERIMENTAL STUDY

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It is common knowledge among surgeons that calculi in the common bile duct are frequently overlooked. Consequently, the common duct is explored at the time of cholecystectomy in an increasing percentage of cases. The exploration is not considered complete unless the patency of the papilla of Vater is proved, and this step is often combined with systematic instrumental dilation of the papilla. The methods used for dilation differ somewhat in the type of instrument and in the amount of distention recommended. The dilators employed have been in most instances either soft woven catheters [1] or metal probes with olive tips (Bâkes).[2] It is the purpose of this paper to describe a series of experiments planned to reproduce as nearly as possible in the experimental animal the conditions of the operation. The immediate and late effects of dilation with both types of instruments have been studied, and the influence of various factors has been evaluated. The clinical significance of these studies has been discussed elsewhere.[3]

Dogs were chosen as experimental animals because the papilla and intramural portions of the common bile duct of the dog more nearly resemble the corresponding regions in man than do those of any other animal commonly used in the laboratory.[4] Although the common bile duct and the pancreatic ducts of the dog open into the intestine separately, there is a musculus proprius two layers thick about the papilla

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1. Cheever, D.: Instrumental Dilatation of the Papilla of Vater and the Dislodgment of Calculi by Retrograde Irrigation, Arch. Surg. **18**:1069-1077 (April) 1929.

2. Allen, A. W., and Wallace, R. H.: Technique of Operation on the Common Bile Duct, Am. J. Surg. **28**:533-561, 1935.

3. Zollinger, R.; Branch, C. D., and Bailey, O. T.: Instrumental Dilatation of the Papilla of Vater, Surg., Gynec. & Obst. **66**:100-104, 1938.

4. Boyden, E. A.: The Sphincter of Oddi in Man and Certain Representative Mammals, Surgery **1**:25-37, 1937.

and the intramural portion of the duct (fig. 1). In the dog, Boyden [4] found that almost the entire intramural course of the bile duct is encircled by scattered loops of smooth muscle. The most distal of these loops he found to be thicker and more isolated than the rest. Hence he felt that these muscles may be regarded as a subterminal sphincter choledochus, or subterminal ring. Lueth [5] in studying the intramural pressure gradient of large, anesthetized dogs described a special sphincter

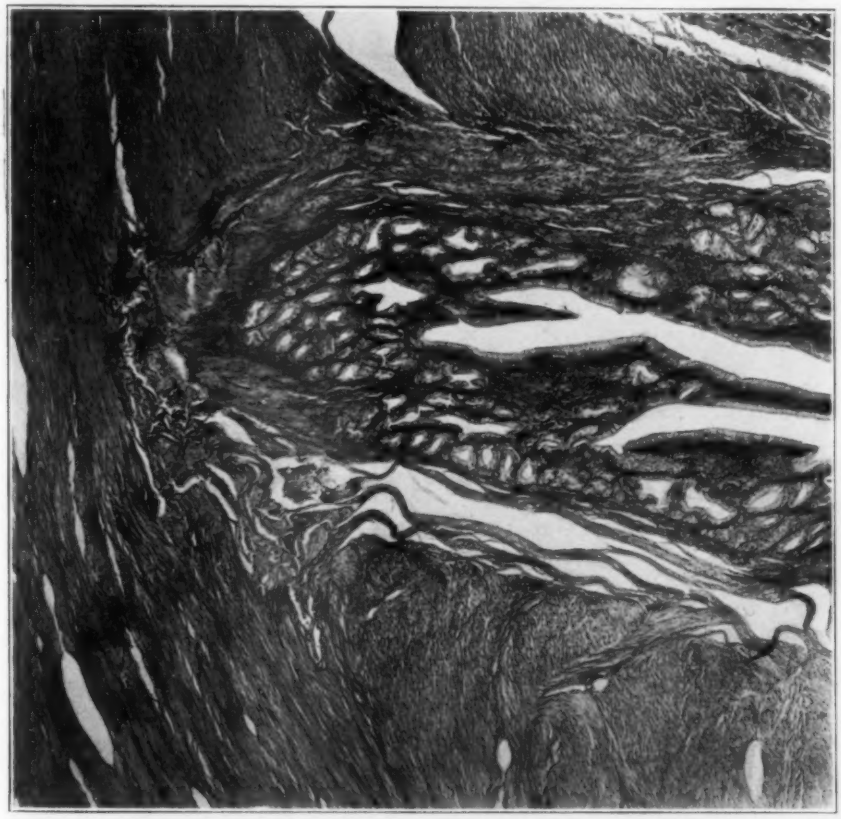

Fig. 1.—Normal papilla of Vater of a dog (× 13) showing intact layers of musculature distinct from that of the duodenal wall. (Reproduced by permission of *Surgery, Gynecology and Obstetrics.*)

of the papilla which exerted one third to one sixth of the total resistance offered to the flow of fluid through the intramural portion of the common bile duct. He called attention to the bulging of the papilla before the threshold level at which fluid flowed into the duodenum was reached. He regarded this as evidence of a true terminal sphincter. We have

5. Lueth, H. C.: Studies on the Flow of Bile into the Duodenum and the Existence of a Sphincter of Oddi, Am. J. Physiol. **99**:237-252, 1931.

seen this to be a constant finding in procedures for determining ductal and perfusion pressures during operations in which the duodenum has been opened.

METHOD

Experiments were carried out on 63 dogs for the purpose of studying the effects of various procedures on the biliary system. In one group the papilla of Vater was dilated through the stump of the cystic duct, while in the remaining groups it was dilated by the transduodenal approach. Because of the relative size of the cystic and common bile ducts in the dog it is impossible to pass an instrument sufficiently large to dilate the papilla to the desired extent. Since it has long been established that cholecystectomy causes some dilatation of the ductal system, it was thought advisable to carry out certain of these procedures with and without cholecystectomy in order to determine how important a role cholecystectomy itself played in the production of the final results. The size of the papilla of Vater in normal dogs varies to some extent with the size of the animal. We have accepted a diameter equal to that of a no. 10F catheter as representative of the average size for the large dogs used in this laboratory.

In most cases, at the time the dogs were killed, roentgenograms were taken after injection of iodized oil into the biliary tract. This was done in order to determine the amount of dilatation of the ductal system that took place after the various operative procedures. Figure 2 shows a normal biliary tree as outlined in this way. Attention is called to the fine radicles, which are the intrahepatic ramifications of the system. Only a few of these radicles are filled with the injection mass in this normal specimen.

Histologic studies were made in all instances. Changes were sought in the papilla of Vater, in various portions of the common bile duct, in the extrahepatic ducts and in the intrahepatic ductal system. The appearance of the liver at the time the animal was killed was compared with that of tissue taken for biopsy at the time of operation.

GROUP 1.—*Cholecystectomy alone.*

As has been mentioned, cholecystectomy alone has long been known to cause a certain amount of dilatation of the extrahepatic ductal system. In order to determine the extent of this factor under the conditions of our experiments, we performed cholecystectomy on 6 dogs. Biopsy of material from the liver was done at the same time in order that the tissues taken for biopsy might later be compared with that obtained at postmortem examination. The dogs were killed one hundred and twenty days after operation. Grossly there had been slight dilatation of the papilla of Vater and of the extrahepatic ductal system. The size of the papilla was found to average the size of a no. 14F catheter, and that of the common bile duct, that of a no. 19F catheter. A roentgenogram (fig. 3) taken after injection of iodized oil into the biliary system confirmed the enlargement of the common bile duct. Note the bulbous dilatation of the remnant of the cystic duct, indicated by the arrow. There was, however, only a slight increase in size of the larger intrahepatic ducts. The terminal ones appeared much the same as in the normal control animal. Microscopic examination showed some flattening of the villi of the common bile duct. There was no inflammatory reaction in the region of the common bile duct or the papilla of Vater. Specimens for biopsy taken from the liver at the time of cholecystectomy and those obtained at the time the animal was killed were normal in appearance.

Fig. 2.—Roentgenogram of the biliary tree of a normal animal after injection of iodized oil.

Fig. 3.—Roentgenogram showing slight dilatation of the intrahepatic ducts of an animal after cholecystectomy. The arrow points to the bulbous remnant of the cystic duct.

Fig. 4.—Roentgenogram showing the effect of cholecystectomy followed by dilation of the papilla through the cystic duct. Note the extreme dilatation of the extrahepatic system.

Fig. 5.—Photomicrograph (× 110) of the common duct of an animal in which dilation was done through the cystic duct. The villi are flattened, and there is increased connective tissue with no evidence of inflammation.

GROUP 2.—*Cholecystectomy; dilatation of the papilla through the cystic duct.*

In this group an attempt was made to dilate the papilla of Vater through the stump of the cystic duct after cholecystectomy. Seven dogs were used. Obviously it was impossible to dilate the papilla greatly without damaging or tearing the common bile duct beyond repair. In 2 of the dogs, the catheter introduced was no. 16F. In the remainder, no. 14 or no. 12F was used. The animals were killed on an average of one hundred and twenty-five days after this procedure. The papilla was found to be enlarged slightly (to the diameter of a no. 14F catheter on the average). An unexpected finding was the extreme dilatation of the extrahepatic ducts. This was more marked than in any other group in the series. The average diameter of the common bile duct was equivalent to that of a no. 28F catheter. Roentgenograms taken after injection of iodized oil into

Fig. 6.—Roentgenogram showing generalized increase in the size of the ductal system following transduodenal dilation by catheter.

the biliary system confirmed the striking dilatation of the common and extrahepatic bile ducts (fig. 4). There was slight enlargement of the larger intrahepatic ducts and of the terminal radicles. Microscopic examination showed some dilatation of the papilla; there were thickening and fibrosis of the wall of the common bile duct (fig. 5). The lining of the common duct was greatly flattened, although in some regions a few villi persisted. Biopsy of specimens taken from the liver at the time of operation showed normal tissue. Autopsy specimens of the liver showed a slight increase in the periportal connective tissue, and moderate numbers of lymphocytes were found in that region.

GROUP 3.—*Cholecystectomy; transduodenal dilatation of the papilla with catheters.*

In this group there were 7 dogs. Cholecystectomy was followed at the same operative session by transduodenal dilation of the papilla to the no. 18F size

by means of soft woven catheters. Biopsy of material from the liver was done in each instance. After an average of ninety-six days the dogs were killed. At this time there was some dilatation of the extrahepatic ductal system, with slight thickening of the walls. The roentgenogram (fig. 6) demonstrated only slight increase in the size of the larger ducts. In this specimen the stump of the cystic duct was strikingly dilated. An increase in the number of visible intrahepatic radicles was noted, and all appeared slightly larger than normal. The papilla of Vater was found to have returned to the size of a no. 10F catheter on the average, and the common bile duct had increased in size to that of a no. 21F catheter. Microscopic examination showed an increase in connective tissue about the papilla. In the common bile duct the villi were flattened, and there was slight increase in fibrous tissue, but no inflammatory reaction was noted. Biopsy specimens taken from the liver at the time of the operation were normal. Those obtained at the time of the animals' death showed a slight increase in the periportal connective tissue. The microscopic sections also demonstrated the dilatation of the intrahepatic bile ducts indicated by the roentgenograms.

Fig. 7.—Roentgenogram showing an increase in size of the intrahepatic ducts with slight increase in size of the extrahepatic system following dilation with metal dilators.

GROUP 4.—*Cholecystectomy; transduodenal dilation of the papilla with Bâkes dilators.*

A group of 5 dogs was used to study the effects of the Bâkes dilators on the biliary system. Cholecystectomy was carried out; then the duodenum was opened, and the papilla of Vater was dilated transduodenally with the Bâkes instruments to a diameter equal to that of a no. 17F catheter. On an average of sixty-three days after the operation the animals were killed. It was found that the papilla had returned to approximately normal size, the average being equivalent to that of a no. 12F catheter. The diameter of the common duct at this time was found to be that of a no. 16F catheter. A roentgenogram (fig. 7) taken after injection of iodized oil showed some enlargement of the extrahepatic system as well as an increase in the number of small intrahepatic ducts which were demonstrable

after the injection. There were also an enlargement of the larger intrahepatic ducts and an apparent clubbing of their terminal injected portions. Microscopic examination showed changes similar to those in the preceding group. There were slight scarring in the region of the papilla of Vater, flattening of the villi in the common bile duct and a minimal increase of periportal connective tissue in the liver.

GROUP 5.—*Cholecystectomy; dilation of the papilla with Bâkes dilators; drainage of common bile duct.*

In an effort to simulate in another respect the procedure usually carried out in man, the common bile duct was drained in 4 animals. After cholecystectomy had been performed a catheter was introduced into the common bile duct through the stump of the cystic duct and was anchored firmly in place. The duodenum was then opened, and the papilla of Vater was dilated with the Bâkes dilators to the diameter of a no. 21F catheter. After ninety-two days the animals were killed. It was found that the diameter of the papilla was equal to that of a no.

Fig. 8.—Roentgenogram of an animal in which the common duct was drained after cholecystectomy. Dilation was carried out by transduodenal approach. Generalized, though slight, ductal dilatation is present.

11F catheter on the average. There was inflammatory reaction about the common bile duct in all of the animals, but there was no evidence of compression or stricture of it. A roentgenogram (fig. 8) taken after injection of iodized oil showed a definite increase in size of the extrahepatic bile ducts but only a very slight increase in size of the intrahepatic ducts. The microscopic appearance of the papilla and intramural portion of the duct in most places did not vary from the normal, and there was only slight scarring in a rare field. The common bile duct was dilated; the villi were flattened, and there was a considerable increase of connective tissue with lymphocytic infiltration. The liver showed slight increase in periportal connective tissue, but there were no inflammatory changes.

GROUP 6.—*Cholecystectomy; dilation of the papilla after an interval.*

This group was studied in order that dilation of the papilla of Vater might be carried out in a biliary system already rendered pathologic by the preceding

operation. Multiple operations on the human biliary system are by no means rare. This was designed as a test to see whether such operations produce more marked effects than do similar procedures when carried out at one operation. Cholecystectomy was performed as a preliminary operation on a series of 6 dogs. Two hundred days after the original procedure the papilla was dilated transduodenally so that the average diameter was that of a no. 20F catheter. The animals were killed one hundred days after the second operation. It was found that the papilla had returned on an average to the diameter of a no. 12F catheter. There was a slight increase in the size of the common bile duct and of the intrahepatic ducst, as seen in the roentgenograms. Slight scarring was present in the intramural portion of the ductal system. There was flattening of the villi in the common bile duct.

GROUP 7.—*Cholecystectomy; dilation of the papilla; redilation after an interval.*

With 5 animals dilation was performed on two occasions. This was done in order to determine the effects of a second dilation on a papilla which had had previous trauma. The procedure in this group was an extension of that used in group 6 so that the second operation was performed on an extrabiliary system already altered by the first dilation as well as by the cholecystectomy. At the first operation cholecystectomy and biopsy of material from the liver were performed. At the same session the papilla of Vater was dilated to an average size equal to that of a no. 17F catherter. This was done by means of a soft woven catheter by transduodenal approach. One hundred and forty days after the first operation a second operation was carried out. The duodenum was again opened. The papilla of Vater at this time was found to have returned to the normal size (that of a no. 10F catheter); it was then dilated to the no. 20F size. When the animals were killed, one hundred days after the second operation, the papilla was found to be somewhat enlarged, measuring the same as a no. 14F catheter on the average. The common bile duct in all instances showed gross evidence of inflammatory reaction. Its average diameter was that of a no. 23F catheter. A roentgenogram (fig. 9) of the biliary system showed the extrahepatic ducts to be greatly enlarged in 4 dogs but not in the fifth. In this animal they were thick walled, and there was considerable stenosis of the duct in its midportion. On the whole, roentgenograms demonstrated an increase in size of the intrahepatic ducts, particularly in the medium-sized ones. The injected intrahepatic ducts were also more numerous than in control animals. Microscopic examination in each instance showed considerable alteration in the region of the papilla of Vater. The normal contours of the muscle bundles were broken up and the intervals filled with dense but well vascularized collagenous tissue. No areas of recent hemorrhage were seen. There were some phagocytes filled with hemosiderin granules in scattered areas. The common bile duct in each case showed dilatation and flattening of the villi. There was moderate lymphocytic infiltration and increase in connective tissue in both the submucosa and the muscularis. Comparison of the biopsy specimens taken from the liver at the first operation with sections obtained after death of the animal showed an increase in the periportal connective tissue. This was accomplished by lymphocytic infiltration and a deposit of hemosiderin in phagocytes in that region. The small intrahepatic ducts were all dilated, but the degree of dilatation varied considerably from specimen to specimen.

GROUP 8.—*Dilation of the papilla without previous cholecystectomy.*

Since it had been shown by previous investigation that there is an enlargement of the papilla of Vater and the common bile duct after cholecystectomy

alone, dilation of the papilla of Vater was carried out with a group of 8 dogs on which no previous operation had been performed. Catheters were used for dilation in 5 dogs, the papilla being dilated transduodenally to a diameter equal to that of a no. 21F catheter. The Bâkes instruments were used in 3 dogs, dilation being carried to the no. 23F size. The animals were killed at intervals varying from one hundred and twenty to one hundred and sixty days after the operation. It was found that the papilla had returned to the diameter of the no. 10F catheter. The common bile duct in all instances presented enlargement, averaging in diameter the size of a no. 20F catheter. Roentgenograms taken after injection of iodized oil showed slight enlargement of the extrahepatic ducts, but there was very little increase in size of the intrahepatic ductal system. With some of these dogs the biliary system presented a nearly normal appearance, the type of instrument used for dilation apparently having no effect on the final result. Microscopic examination showed only slight scarring of the papilla, several of the sections appearing normal. There was some slight dilatation of the

Fig. 9.—Roentgenogram of the biliary tract of an animal in which the papilla was dilated on two occasions. There is an increase in size of the extrahepatic and larger intrahepatic ducts.

common bile duct, and scarring of its wall was minimal. The villi were still visible, though less prominent than normal. In an occasional field there was slight increase in the periportal connective tissue of the liver. Occasional lymphocytes were present in this region, and some slight enlargement of the terminal bile ducts could be detected.

GROUP 9.—*Experiments to show the early effects of dilation of the papilla.*

The early effects of dilation of the papilla were studied in a group of 15 dogs. Dilation was carried out with soft woven catheters by the transduodenal approach. Cholecystectomy was not performed. The dogs were killed at intervals varying from one to twenty-eight days. Gross examination at the time of death showed that in the first week the papilla was large and edematous, protruding into the lumen of the duodenum. No attempt was made to measure the actual

size in order to obtain microscopic sections of papillae which had had no other trauma than that occurring at the time of the original dilation. In the specimens obtained one to three days after dilation the continuity of the epithelium was broken in many places, and these areas were sealed with fibrin and polymorphonuclear leukocytes. The exudate was so extensive as to fill the lumen almost entirely (fig. 10). In addition, there were extensive areas of hemorrhage in the surrounding tissue. Portions of the mucosa which were not eroded showed edema and infiltration with polymorphonuclear leukocytes. At the end of a week the lumen of the papilla had reached approximately normal size, and most of

Fig. 10.—Photomicrograph (× 90) of the papilla of Vater three days after dilation. The lumen is filled with fibrin and leukocytes. The mucosa is interrupted, and there is acute inflammatory reaction beneath it. (Reproduced by permission of *Surgery, Gynecology and Obstetrics.*)

the exudate had disappeared. The continuity of the epithelium was partially restored. In the mucosal stroma there were many lymphocytes, but polymorphonuclear leukocytic reaction was slight. There were many young fibroblasts and some newly formed capillaries throughout the mucosa and in the layers of muscle ensheathing the papilla. Sometimes these even extended into the adjacent intestinal musculature for a short distance. At the end of one month, connective tissue richer in collagen had taken the place of the fibroblasts. It extended at various points through the investing musculature for a short distance. The mucosal

epithelium was complete, but the glands appeared somewhat altered in outline, and in the stroma about them were numerous lymphocytes and some plasma cells.

COMMENT

The series of experiments on these 63 dogs forms a basis for discussion of the results of various manipulations on the biliary system. The results in the various groups offer evidence which may promote understanding of the results of different types of surgical procedures. Dilation of the papilla of Vater was accomplished through the stump of the cystic duct and also by the transduodenal approach. When it was carried out through the stump of the cystic duct, a large amount of dilatation of the extrahepatic ducts was found at the time of the animal's death. The trauma from instrumentation at the time of operation in this group must have caused considerable damage to the lining of the common bile duct, for sections showed rather extensive scarring. Whether this was due to trauma to the interior of the duct alone or whether injury to the nerve supply of the duct as a result of the dilation was an added factor can not be determined from these experiments. At least, one can be certain that the scarring was localized to the region of the trauma. The papilla of Vater and the intrahepatic ducts appeared both grossly and microscopically normal at the end of one hundred and twenty-five days.

In the remaining groups of experiments, dilation was performed after the duodenum had been opened. The amount of scarring in the region of the papilla and the effect on the other portions of the ductal system varied considerably. In one group there resulted severe damage which could be attributed only to the dilation. This was group 7, in which dilation was performed on two occasions. Uniform and extensive scarring of the region of the papilla with pathologic change in the other portions of the biliary system was a constant finding. There was a definite increase in the periportal connective tissue of the liver. The amount of scarring in the various groups did not seem to be affected by the type of instrument used. Much the same results were obtained with the soft woven catheter as with the metal bougie (Bâkes instrument). The findings in group 5 (in which the common duct was drained by a catheter) were of especial interest. In spite of some inflammatory reaction about the common bile duct there was only slight dilatation of the extrahepatic ducts, and the villi, though flattened, were distinct in most sections. The remaining portions of the ductal system were likewise essentially normal in appearance. This would suggest that drainage of the common bile duct has little permanent deleterious effect on that structure or on other parts of the extrahepatic biliary passages and may, indeed, through reduction in pressure caused by the

block at the papilla immediately following the trauma of dilation, actually be a factor in preventing permanent increase in the size of the ductal system.

In the dogs which showed extensive scarring in the region of the papilla a definite increase in size of the intrahepatic ducts was also observed. This would suggest an increased intraductal pressure.

In the group in which the animals were sacrificed from one to twenty-eight days after dilation of the papilla there can be no doubt that the edema and exudate caused considerable obstruction of the papilla. The edema subsided at the end of approximately a week, and the papilla returned to normal size. Thus, during this period, it is doubtful whether dilation could result in any increase in the lumen of the papilla of Vater unless there had been extensive tearing of the entire intramural portion of the duct. Then there would exist a free

Instrumental Dilation of the Papilla of Vater

Type of Experiment	No. of Animals	Survival, Days	Papilla Dilated to	Size of Papilla
Control	..	...	....	10 F
Cholecystectomy	6	120	....	14 F
Cholecystectomy; dilation through cystic duct	7	125	14 F	14 F
Cholecystectomy; catheter dilation	7	96	18 F	10 F
Cholecystectomy; Bâkes dilation	5	63	17 F	12 F
Dilation; common duct drainage*	4	92	21 F	11 F
Dilation 200 days after cholecystectomy	6	100	20 F	12 F
Dilation 140 days after primary dilation*	5	100	(1) 17 F (2) 20 F	10 F 14 F
Dilation without chilecystectomy	8	140	22 F	10 F
Acute experiments	15	1-28	22 F	

* Cholecystectomy also performed.

communication with the duodenum, devoid of a sphincteric mechanism. Such an extensive laceration of this region might allow the entrance of bacteria into the tissues and lead to infection of the region. It would ultimately result in scarring, and stricture might result if contraction were sufficiently great. At any rate, the physiologic action of this region would be interfered with to a great extent by this procedure.

From the standpoint of the surgeon, the purpose in dilating the papilla of Vater extensively is to render its lumen larger so that unnoticed calculi may pass spontaneously.[3] The results of these experiments suggest that shortly after operation the lumen fills with exudate if the papilla has been dilated to a large size. This was confirmed by our studies of intraductal pressure, reported elsewhere.[3] Furthermore, the experiments indicate that when this stage passes the lumen returns to its original size regardless of the extent to which it was dilated at operation. Thus, extensive dilation of the papilla does not enlarge the lumen either shortly after operation or later.

CONCLUSIONS

1. Obstruction of the papilla of Vater after its dilation occurs during the first week as a result of the exudate in the duct and the edema of the surrounding tissues.

2. A certain degree of scarring in the region of the papilla of Vater occurs after extensive dilation. This was moderate to marked in 50 per cent of the experimental animals in the present series.

3. Dilatation of the extrahepatic bile ducts occurred to some extent in all groups. This seems to be influenced by the amount of scarring about the papilla rather than by the method or instrument used.

4. Dilatation of the extrahepatic bile ducts seems somewhat lessened when drainage of the common bile duct is instituted.

5. When portions of the cystic duct are left at cholecystectomy, they dilate to form a pocket of considerable size.

6. Increase of periportal connective tissue and dilatation of the intrahepatic bile ducts were both proportional to the degree of scarring of the papilla of Vater.

7. The size of the papilla of Vater after dilation by various methods remains essentially the same as the initial size. Dilation thus results in no permanent enlargement of the papilla of Vater.

8. These investigations lend support to the view that no further dilation of the papilla of Vater should be carried out in human patients after its patency has been ascertained.

CORRECTION

In the article by Dr. Deryl Hart entitled "Sterilization of the Air in the Operating Room by Bactericidal Radiant Energy: Results in over Eight Hundred Operations," in the December issue (ARCH. SURG. **37**:956, 1938), in the third sentence of the paragraph beginning "This report," at the top of page 957, "The operations in the present series" should have read "The latter operations;" i. e., the operations referred to are those in which there was a potential source of infection.

REVIEW OF UROLOGIC SURGERY

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KIDNEY

Anomalies.—Jasienski [1] called attention to a case in which there was congenital aplasia of the left kidney, the organ being minute and functionless, while the right kidney was an enormous hydronephrotic sac with a large calculus in its pelvis. At necropsy the aplastic organ was found to contain no trace of renal tissue; the entire structure was composed of a series of cystic cavities filled with yellowish serous fluid. Congenital renal aplasia or hypoplasia of such high grade as to deprive the kidney of all functional value is rather rare. Although Ballowitz (1895) collected 213 and Gerard (1905) 278 cases among 527 congenital malformations of the kidney, it is probable that in a great many of these cases the true condition was solitary kidney or double kidney or that the two kidneys were fused on the same side.

It is frequently impossible, especially if necropsy is not performed, to know whether the condition under observation is congenital aplasia, hypoplasia of high grade or secondary atrophy of a kidney. Frequent references in the literature stress the importance of removing a func-

1. Jasienski, G.: Contribution à l'étude des affections du rein unique; un cas d'hydronéphrose calculeuse géante chez un sujet avec atrophie du rein opposé, J. d'urol. **45**:45-50 (Jan.) 1938.

tionless kidney, but mention is seldom made of diseases of the opposite kidney (properly called a solitary kidney), their frequency, their evolution and their outcome. Not infrequently evidence is found that solitary kidneys have been removed. In cases in which functional examination and ureteral catheterization do not give adequate information there is good reason to follow Rovsing's advice to perform exploratory lumbotomy not only when it is uncertain which kidney is affected but when it is impossible to exclude with certainty the possibility of hypoplasia of one kidney. Among the 213 cases of aplasia or hypoplasia collected by Ballowitz the opposite kidney was reported to be of increased size in 55 cases, and in 25 cases chronic nephritis or hydronephrosis was observed. In 16 cases hydronephrosis was due to stone in the kidney or ureter.

It is evident that in such cases obstruction of the ureter by a stone or by a kink due to compression by a large cyst is necessarily followed by fatal anuria and uremia. In the author's case anuria was the final result of a stone in the distended renal pelvis, which from time to time, with changes of position, caused obstruction by its weight. The astonishing thing was that the 26 year old patient lived as long as she did without urinary disturbances. The case shows what minute vestiges of renal parenchyma may suffice to maintain life.

Roentgen evidence of absence of a kidney may indicate previous surgical removal, renal destruction resulting from disease or congenital absence; the remaining kidney, therefore, may be regarded as either a congenital or an acquired solitary kidney.

Braasch and Merricks [2] review the clinical findings in 27 cases of proved renal agenesia (operation, 14; necropsy, 13) and in 42 cases in which the diagnosis was inferred from roentgenographic and cystoscopic data. These findings were compared with those in cases of acquired solitary kidney. The most common subjective symptom of renal agenesia was pain on the side on which the kidney was present. The most common objective evidences found on physical examination were a palpable mass on the side on which the kidney was present (24 per cent) and tenderness to palpation (16 per cent).

As might be expected with renal anomalies, secondary complications were present in the congenital solitary kidney in 43 of the 69 cases. In order of frequency they were pyelonephritis, anomalies of form and position, hydronephrosis, lithiasis, nephritis and tuberculosis.

From roentgenographic data the size and position of the kidney, the size of the renal pelvis and the width and definition of the psoas

2. Braasch, W. F., and Merricks, J. W.: Clinical and Radiological Data Associated with Congenital and Acquired Single Kidney, Surg., Gynec. & Obst. **67:** 281-286 (Sept.) 1938.

muscle were noted and compared with similar observations in 33 cases of acquired solitary kidney. It was found that the congenitally solitary kidney is enlarged in 90 per cent of cases and that this enlargement is present more frequently and is distinctly greater than in cases of acquired solitary kidney. Enlargement of the pelvis of the congenitally solitary kidney was not commensurate with that of the parenchyma; the size differed little from that of the pelvis of the acquired single kidney. The congenitally solitary kidney tends to occupy a position lower than that taken by the kidney which undergoes compensatory hypertrophy after nephrectomy, and this sign may be regarded as a definite factor in identifying this condition. The shadow of the psoas muscle was wider on the side on which the kidney was absent than on the other side in 16 per cent of cases of agenesia; of 100 consecutive urograms, the shadows were of equal width in 99. A more common finding in cases of agenesia was absence of definition of the psoas shadow on the side on which the kidney was absent (40 per cent). There was a difference in definition on comparison of the two sides in only 16 per cent of a series of 100 unselected urograms.

Stone.—Grosperrin [3] on the basis of 2 illustrative cases of lithiasis associated with tuberculosis of long standing stated that tuberculosis has a marked effect on calcium metabolism, leading invariably to more or less violent decalcification, revealed by increase of calciuria. It is normal for urine rich in calcium salts to have a tendency to deposit these in the form of concretions. Although hypercalciuria is not of any special pathologic importance in every case of tuberculosis, it has marked significance in cases in which tuberculosis has attacked the skeleton.

In the first case reported the lithiasis did not appear until six years after the first symptoms of Pott's disease. While it is impossible to say with certainty whether the mild infection (bacteriuria rather than pyuria) preceded or followed the formation of stone, the friability of the calculus and its granular appearance suggested secondary lithiasis and permitted, with some degree of probability, incrimination of the infection.

On the other hand, uric or uratic lithiasis, such as was present in the author's second case, seemingly develops by a different humoral mechanism. In this case the patient was suffering with florid pulmonary tuberculosis of slow evolution, and nothing in the bony portion of the skeleton indicated any noteworthy decalcification. Yet he was suffering with attacks of renal colic and hematuria and was found on examination to have a small calculus in the left renal pelvis, for which operation

3. Grosperrin: La lithiase rénale chez les anciens tuberculeux, J. d'urol. **45:** 199-204 (March) 1938.

was performed. Grosperrin raised the medicolegal question whether a renal stone discovered some years afterward in a case of arrested tuberculosis should be regarded as the result of tuberculosis. An increasing number of cases seems to indicate that there is a clear relation of cause and effect between tuberculosis, with its necessary treatment by superalimentation, and renal lithiasis.

The immediate results of the "V" type of nephrotomy, described by Prather [4] in 1934, proved to be satisfactory. He reviewed the condition of the patients, and particularly of the kidneys, after several years to see if the results justified the procedure.

The follow-up data on 6 kidneys operated on approximately three to five years before justified their being regarded as a group and allowed certain conclusions to be drawn. All of the 5 patients were in good general health. None had pain or symptoms referable to the side on which operation was done.

Stones had not formed in the opposite kidney after operation. Marked recurrence of stone had taken place in 2 of the 6 kidneys which had been operated on. The p_H of urine from 1 kidney, in which recurrence of stone was extensive, was 8.

Four of the 6 kidneys were known to have been infected before operation. Of the 4 kidneys in which there was little or no recurrence of stone, in 2 there was no infection and in the other 2 mild bacilluria without pus. The p_H of the urine from 2 of those kidneys which had remained free of stone was given as 5.5 and 7.0 respectively.

None of the patients had followed an adequate medical program for stone since operation. Prather expressed the belief that with increased interest and knowledge regarding the formation of stone and prevention of recurrence and with intelligent application of the newer urinary antiseptics, results of renal surgical procedures for stone should be definitely improved.

Higgins [5] reviewed 100 cases of recurrent renal lithiasis and stressed the necessity of a conscientious postoperative regimen.

The left kidney was the site of recurrence in 40 cases and the right in 32. Recurrence was bilateral in 28. Recurrence developed most frequently in the first three years after operation in the cases in which recurrence was unilateral and in the first eight years after operation in the cases in which recurrence was bilateral. Staphylococcus albus was the organism most frequently associated with recurrence; the organism next most frequent was of the genus Proteus.

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4. Prather, G. C.: Review of the "V" Type Nephrotomy for Staghorn Calculus with Special Reference to Final Results, Am. J. Surg. **39**:589-601 (March) 1938.

5. Higgins, C. C.: Recurrent Renal Lithiasis: Review of One Hundred Cases, Tr. Southwest. Br. Am. Urol. A., 1937, pp. 2-10.

Deficiency of vitamin A was indicated by a positive reaction to the biophotometer test in 68 to 72 per cent of cases.

Nephrectomy was performed in 22 per cent of cases because of poor function or marked destruction of the kidney. Two hundred and twenty-three operations had been performed on this group of 100 patients with recurrent lithiasis of the upper part of the urinary tract.

Bailey and Eberhart [6] briefly reviewed the 8 cases in which renal calculi have been reported to weigh more than 300 Gm. The largest surgically removed stone weighed 1,440 Gm. In Bailey and Eberhart's case nephrectomy was performed with considerable difficulty. The stone weighed 1,565 Gm. Chemical analysis of the stone revealed calcium, magnesium, phosphates, carbonates and a trace of sulfur and oxylates. There were no urates. The patient recovered from the operation.

Von Illyés [7] stated that in cases of bilateral renal stone and in cases of solitary kidney, operation should not be delayed until renal insufficiency has developed, or, if it does develop, operation should be carried out while the insufficiency is in progress. The earlier the operation is performed, the more renal parenchyma can be saved.

Even in the presence of the most extreme involvement every detail of the patient's condition should be considered and the need for surgical intervention determined. Renal insufficiency in cases of desperate involvement can be bettered only by removing the stone which is causing the obstruction and infection. Nonoperative treatment usually eventuates in death of the patient.

Chaton [8] reported a case in which transperitoneal extraction of a calculus from one pelvis of a horseshoe kidney was effected. The first roentgenogram in this case (hematuria was present) resulted in a diagnosis of probable calculus of the right renal pelvis; the kidney therefore was approached by the usual lumbar incision. The organ was found in a position abnormally oblique from above downward and from without inward. The lower pole was astride the vertebral column. The internal contour of the kidney could not be made out, and it became apparent that the organ was continuous, across the median line, with the parenchyma of the other kidney. A diagnosis of horseshoe kidney was made. Débridement in the region of the pedicle, which was displaced in the median portion, was difficult in front. Vascularization was abnormal and intricate. At no point could any mass of calculous

6. Bailey, M. K., and Eberhart, C. A.: Large Renal Calculus, J. A. M. A. **111**:610-612 (Aug. 13) 1938.

7. von Illyés, G.: Ueber die Insuffizienz bei Steinniere, Ztschr. f. urol. Chir. u. Gynäk. **44**:63-73, 1938.

8. Chaton, M.: Extraction d'un calcul du bassinet par voie transpéritonéale dans un cas de rein en fer-a-cheval, J. d'urol. **45**:56-59 (Jan.) 1938.

consistency be palpated. In view of the difficulties involved in further exploration it seemed prudent to terminate the operation, closing the wound without drainage.

After some weeks of rest in bed all symptoms disappeared, and the patient was dismissed from the hospital. One year later the hematuria recurred. A roentgenogram again revealed a calculus of the pelvis of the right kidney. Owing to the difficulties encountered by the lumbar approach at the first operation, the kidney was exposed by the transperitoneal route. A horseshoe kidney, with isthmus at the lower poles, was revealed. Within the upper right portion of the organ, in what appeared to be the pelvis, was a sclerolipomatous mass the size of a hen's egg. Below this was a canal 3 cm. in length, resembling a ureter but leading into a second, abnormal pelvis on the same side. Incision of this lower pelvis revealed a stone the size of a walnut, which was removed. The sclerolipomatous tumor was not destroyed but was utilized to reenforce the suture. This tumorous mass, with well defined outlines, had developed from the center of irritation and chronic inflammation caused by the stone.

In operative intervention on a horseshoe kidney the extraperitoneal route of approach, recommended by Gutierrez, Papin and others, would seem to give the most satisfactory results. Occasionally, however, there are unusual circumstances in which a transperitoneal operation gives a better result.

Hydronephrosis.—Eichelberger [9] produced experimental hydronephrosis by increased intraureteral pressure resulting from partial constriction of the ureter. Experimental hydronephrosis has been classified into two goups: the chronic form, in which approximately 50 per cent of the renal tissue is destroyed, and the progressive form, in which the greater part of the renal tissue is destroyed. Chemical studies of the blood serum of animals with the chronic condition disclosed no significant deviation from the normal. In animals with the progressive condition the following significant changes were found in the uremic stage: marked acidosis; retention of nonprotein nitrogenous constituents, and increased concentrations of calcium and inorganic phosphorus, unaccompanied by any change in the total concentration of protein but accompanied by an increased albumin-globulin ratio.

Tumors.—Soloway [10] reported a series of 130 cases of renal tumor. In 90 cases the growth was discovered at operation and in 45 at necropsy.

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9. Eichelberger, L.: Experimental Hydronephrosis in Dogs: I. The Composition of Blood Serum, J. Urol. **40**:366-377 (Sept.) 1938.

10. Soloway, H. M.: Renal Tumors: A Review of One Hundred and Thirty Cases, J. Urol. **40**:477-490 (Oct.) 1938.

Hypernephroid carcinoma is the most common type of renal neoplasm; it occurred in 91 cases (70 per cent). This type of tumor is characterized by its tendency to invade the renal vein and the vena cava, by its slow, progressive growth and relatively late symptoms and by its tendency to produce hematogenous metastasis. The metastatic growths are formed especially in the lungs and in the bone and often are the first clinical evidence of the disease.

Renal tumors occur more frequently among males than among females (96 to 34) and most often in the fifth and sixth decades of life (75 cases; 57 per cent). The ratio of white to Negro patients was about 8 to 1.

The classic triad of symptoms—hematuria, tumor and pain—occurred in about 20 per cent of cases. The appearance of all three symptoms in the same case nearly always occurred late in the course of the disease, after metastasis had taken place. Hematuria was found in 63 per cent of cases, tumor in 53 per cent and pain in 37 per cent.

Seventeen of the 40 patients who were not operated on did not have any urinary symptoms, and on repeated examination erythrocytes were not found in the urine. The condition of this group of patients was most difficult to diagnose.

Metastasis occurred in 93 per cent of the cases in which necropsy was performed and in about 15 per cent of the cases in which operation was performed.

Nephrectomy, as early and as radical as possible, is the operation of choice. In the presence of ureteral involvement the entire ureter, with a section of the bladder, should be removed. High voltage roentgen therapy should be employed preoperatively and postoperatively in all cases.

Tuberculosis.—Thomas, Stebbins and Petter [11] in discussing the diagnosis and indications for treatment of renal tuberculosis stated that urinalysis should be performed every three months in all cases of tuberculosis.

The destructive lesions of renal tuberculosis can be identified only by means of retrograde pyelograms taken after the pelvis has been well filled with an opaque substance.

As with another type of tuberculosis, there is an early, or "invasion," stage of renal tuberculosis. This period may be symptomless, but careful search will reveal clinical findings that are sufficient for diagnosis. The diagnosis and prompt treatment of the early lesion of renal tuberculosis may prevent the development of renal phthisis.

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11. Thomas, G. J.; Stebbins, T. L., and Petter, C. K.: The Diagnosis and Indications for Treatment of Renal Tuberculosis, Am. J. Surg. **38**:57-65 (Oct.) 1937.

Surgical treatment for any type of tuberculosis (except in an emergency) should not be undertaken until the patient has developed a sufficient defense mechanism. Surgical treatment of urogenital tuberculosis is rarely an emergency procedure. Surgical or medical treatment of tuberculosis should aim at the patient as a whole, not alone at the local lesion.

Renal tuberculous lesions or other urogenital lesions are local manifestations of a constitutional disease. Nondestructive renal tuberculosis, unilateral or bilateral, is a nonsurgical condition and should be treated intensively by medical methods. Bacilli of tuberculosis obtained in one specimen of urine from the renal pelvis do not constitute an indication for nephrectomy.

In cases of early renal tuberculosis, surgeons should be conservative in advising removal of a kidney which eliminates bacilli of tuberculosis unless the pyelogram reveals definite evidence of erosion and unless the urine from the second kidney repeatedly gives negative results when injected into animals.

Unilateral, slightly destructive tuberculosis should be treated conservatively under careful observation. Nephrectomy is indicated only when progressive disease is present. Extensive unilateral destructive lesions should be treated by surgical methods. In cases of bilateral destructive renal tuberculosis operation is not indicated except to stop hemorrhage or to relieve pain and sepsis due to an obstructed ureter.

Tuberculous patients should have careful preoperative treatment.

Heliotherapy is beneficial, but ultraviolet irradiation should be used only in selected instances.

Thomas, Kinsella, Petter and Stebbins[12] stated that the proper surgical treatment of renal tuberculosis is predicated on: (1) a thorough understanding of tuberculosis; where it begins, how it spreads and what measure of resistance the patient has against the bacillus of tuberculosis; (2) an understanding that it is rarely possible entirely to extirpate tuberculosis, so that surgical treatment for renal disease is not aimed at cure but is an aid in obtaining a clinical result; (3) the fact that in more than 50 per cent of all cases in which there are early or late lesions of renal tuberculosis the disease can be arrested in the kidney by medical methods only; (4) the fact that all patients who require surgical treatment for renal tuberculosis recover more quickly if medical treatment is instituted both before and after the surgical treatment than otherwise; (5) the fact that no operative mortality is necessary; (6) the fact that the only complication should be a post-

12. Thomas, G. J.; Kinsella, T. J.; Petter, C. K., and Stebbins, T. L.: Surgical Treatment of Urogenital Tuberculosis, J. Urol. **39**:766-783 (June) 1938.

operative sinal infection or late meningitis, and (7) the fact that if the proper methods of treatment are used ultimate arrest of the infection should occur in 90 per cent of cases.

Lieberthal [13] described the development of the tuberculous renal lesion from its earliest to its end stages by reconstruction of the clinical picture and of the gross and histologic changes in 270 cases of renal tuberculosis.

The tuberculous renal lesion is never primary but is hematogenous, occurring through the medium of embolism. The initial lesions are usually bilateral and because of the peculiarities of the renal circulation are usually cortical. They have a tendency to heal, but occasionally a tubercle will continue to grow. It then breaks into a tubule and discharges organisms, which infect the papilla, producing a papillary ulcer which is the key lesion of renal tuberculosis.

Until the development of the papillary ulcer the disease is latent and cannot be diagnosed clinically. As soon as the caseous papillary ulcer appears, however, there is open tuberculosis with descending infection of the urinary mucous membranes as well as ascending infection of the previously uninvolved portions of the renal tissue. Tuberculous strictures and urinary stasis resulting from the lesion in the mucous membrane play an important part in spread of the renal lesion. The papillary ulcer produces tubular obstruction and a tuberculous cavity which involves the pyramid through a combination of hydronephrotic change and tuberculous erosion.

As a result of the ureteral obstruction the tuberculous urine has a tendency to stagnate in the renal pelvis and to infect the previously uninvolved papilla. Erosion of small vessels with dissemination of tubercle bacilli through the portion of renal tissue supplied by the vessels is an important mode of progression of this type of renal lesion. This produces chains of tubercles extending radially from the eroded part to the surface of the kidney.

Then the original caseous erosion of each renal papilla progresses to formation of large cavities with thin-walled partitions of the columns of Bertini between each two cavities. The stagnant tuberculous urine becomes inspissated, forming the "putty" or "mortar" kidney.

The onset of a secondary infection produces the changes of pyelonephritis and eventually pyonephrosis, with extensive peripelvic and perirenal fibrolipomatosis. Occasionally there is a fulminating infection in which the lesion of the mucous membrane dominates the picture, producing caseous pyeloureteritis.

13. Lieberthal, F.: Renal Tuberculosis: The Development of the Renal Lesion, Surg., Gynec. & Obst. **67**:26-37 (July) 1938.

Although during the latent stage small, isolated tubercles may appear in the opposite kidney, these are not demonstrable clinically but are found at necropsy. It is said that renal tuberculosis usually is clinically unilateral and pathologically bilateral.

The opposite kidney may be, and usually is, finally involved by an ascending infection from involvement of the bladder and ureteral orifice, with consequent ureteral insufficiency and reflux of the tuberculous urine.

Emmett and Braasch [14] stated than an analysis of the methods of diagnosis employed in 100 consecutive cases of proved renal tuberculosis suggested that in more than two thirds of the cases the problem is not to establish the presence of the disease but to determine the degree of involvement of each kidney. Excretory urographic study is becoming more important in this field of diagnosis and is supplanting retrograde pyelographic examination in a large percentage of cases. However, retrograde pyelographic study is still of importance in differential diagnosis in a small group of cases in which the nature of the disease is in doubt and in an occasional case in which the lesion is exceedingly small and circumscribed.

As a result of excretory urographic study, repeated cystoscopic examinations should be entirely unnecessary; one examination will suffice in nearly all cases. A combination of excretory urographic examination, with microscopic examination and staining of the specimen of urine obtained by catheterization of the ureter of the so-called good kidney is no doubt the best procedure to follow at present and supplies sufficiently accurate information in most cases to establish a satisfactory diagnosis and to permit the urologist to decide on the proper treatment.

The most common manifestations in the excretory urogram of the tuberculous kidney, in order of their frequency, are: (1) no visualization; (2) delayed visualization; (3) caliectasis; (4) evidence of necrosis in the outline of the calices; (5) cicatricial deformity of the calices and "pinching off" of the tips of minor calices or obliteration of the calices; (6) deformity or dilatation of the ureter, and (7) pyelectasis.

Jameson [15] studied the incidence of renal tuberculosis among patients with active pulmonary tuberculosis at Saranac Lake. The records of the Saranac Laboratory and of the Trudeau Sanatorium Laboratory

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14. Emmett, J. L., and Braasch, W. F.: Has Excretory Urography Replaced Retrograde Pyelography in the Diagnosis of Renal Tuberculosis? J. Urol. **40**:15-23 (July) 1938.

15. Jameson, E. M.: Renal Tuberculosis in Patients with Active Pulmonary Tuberculosis, Surg., Gynec. & Obst. **67**:56-62 (July) 1938.

were examined to determine how often tubercle bacilli were present in the urine of patients who had pulmonary tuberculosis and whose urine contained other abnormal elements.

The criterion for examination at the Saranac Laboratory was an abnormal number of pus cells in a voided morning specimen of urine, and the criterion at the Trudeau Sanatorium Laboratory was albuminuria. In the latter laboratory, smears were made of sediment from a subsequently obtained twenty-four hour specimen.

It was shown that tubercle bacilli were found much more frequently in smears made from the sediment of the twenty-four hour specimen than from that of the single morning specimen. In only 1 instance was urine which gave a negative smear determined, by inoculation of guinea pigs, to contain tubercle bacilli. This was a twenty-four hour specimen.

In 88 cases of pulmonary tuberculosis in which acid-fast bacilli were found in smears of the sediment of voided urine, inoculation of guinea pigs proved the organisms to be tubercle bacilli (62.3 per cent of the males and 31.4 per cent of the females). Pyuria, albuminuria, erythrocytes and casts were reported to be present twice as frequently in urine containing tubercle bacilli as in urine containing nonpathogenic forms of acid-fast bacilli.

The necropsy records of 239 patients who died from active pulmonary tuberculosis were examined to determine the incidence of renal lesions. A total of 67, or 28.4 per cent (31 per cent of the males and 22 per cent of the females), had renal tuberculosis. In 20.9 per cent this was of the latent, or pathologic, type (nonprogressive, usually miliary), and in 7.1 per cent it was of the clinical, or open, type. The condition was bilateral in 76 per cent of cases of both types. Eighty-eight per cent of the patients with the clinical type of the condition were males. Thus, males not only had a greater tendency to renal tuberculosis than had females, but the patients who had clinical, or advanced, lesions were in the proportion of 3 males to 1 female.

Jameson [15] concluded that careful and repeated search for acid-fast bacilli should be made in smears of the sediment of a twenty-four hour specimen of urine of every tuberculous patient if pus or albumin is present in the urine. In such smears, properly stained, acid-fast organisms can be found in a high percentage of positive cases. In doubtful cases and in all cases in which acid-fast bacilli have been demonstrated, further examination should be made by inoculation of guinea pigs or by culture. Renal tuberculosis was three times as frequent among males with pulmonary tuberculosis as among females with pulmonary tuberculosis in the series of cases under consideration, and the lesions of 76 per cent of the patients were bilateral. Patients with renal tuber-

culosis rarely have "normal" urine, although the presence of tubercle bacilli in the urine depends on the existence of a lesion in communication with the pelvis of the kidney.

Trauma.—Priestley and Pilcher [16] reviewed the records of 45 patients whose kidneys had become ruptured. The majority were young men. Only those cases were considered in which the kidney was ruptured by external violence without penetration of the skin. The type of renal injury varied from slight subcapsular hemorrhage to complete pulpefaction of the kidney. In some cases the ureter or the renal pedicle was completely avulsed. Hemorrhage, usually perirenal but occasionally intraperitoneal, was uniformly present, and hematuria, either gross or microscopic, occurred in 95 per cent of the cases. Leakage of urine around the kidney was common. Serious associated injuries elsewhere in the body were present in 13.3 per cent of cases. Priestley and Pilcher found that healing may occur satisfactorily with medical treatment. On the other hand, urinary fistulas, hydronephrosis, pseudohydronephrosis, pyelonephritis or other anatomic abnormalities may persist or develop. Trauma, hemorrhage and pain are cardinal points to consider in the diagnosis, but they should be substantiated by intravenous urographic examination. In general, medical treatment immediately after the injury is preferred unless it is contraindicated by excessive hemorrhage or by the presence of a large perirenal mass. In certain cases in which patients are treated medically, subsequent operation may become necessary.

The 2 deaths that occurred in this series of 45 cases were attributed to severe extrarenal trauma. Thirty-one patients were followed for periods ranging from four to twenty-six years after injury. Eleven patients who underwent nephrectomy were entirely free of symptoms; 73.7 per cent of those treated medically were entirely well, and the remainder of this group had mild symptoms referable to the urinary tract.

Carbuncle.—Suter [17] discussed the literature on renal carbuncle and reported 5 cases from his own practice. He stated that surgical treatment should be as conservative as possible. In some cases it is impossible for the surgeon to avoid removing the kidney because the differential diagnosis between tumor and abscess cannot be made with certainty. In some cases the situation of the carbuncle makes removal of the kidney necessary.

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16. Priestley, J. T., and Pilcher, F., Jr.: Traumatic Lesions of the Kidney, Am. J. Surg. **40**:357-364 (May) 1938.

17. Suter, F.: Diagnose und Therapie des Nierenkarbunkels, Schweiz. med. Wchnschr. **68**:634-636 (May) 1938.

URETER

Tumor.—Parker [18] pointed out that while many cases of malignant tumor of the ureters have been reported, benign tumors of this organ are relatively rare. He reported a case of papilloma in which the patient was an elderly man who came for observation after a painless hemorrhage of the ureter. A catheterized specimen from the left ureter was composed almost entirely of blood, and the ureter was found to be completely blocked 3 cm. above the bladder. According to the patient, several small stones had been passed two years previously. The left ureterogram revealed a large lacuna in a markedly dilated ureter, above which no opaque substance passed. By intravenous urographic examination the left kidney was shown to be larger than normal, with the lowermost calix compressed from below; observers saw the faint shadow of a cyst which appeared to be attached to the kidney and to be movable with it.

At operation the tumor of the ureter was found to hang like a pendulum by its pedicle at a point in the wall of the ureter above the bladder. Above this point the ureter was atrophied; below it, hypertrophied. Histologically its general structure was that of a papilloma derived from a cylindric epithelioma, formed of an arborescent, fibrous stroma covered with a thick layer of epithelioid cells. Most of the tumor was histologically benign, although at one point there appeared to be infiltration of the stroma by a small group of cells with rather hyperchromatic nuclei; this might suggest malignant transformation. It was possible that this was an oblique section made through the wall of the ureter, where the normal cells are brightly colored. Clinically nothing indicated a malignant tumor. The ureter was not adherent to the walls, and it was easily dissected free. The operative results were excellent, and at the time of Parker's report the patient had completely recovered.

An intensive study of the literature by Chauvin and Cerati revealed reports of 112 cases of tumor of the ureter, of which a third were benign; only 8.3 per cent of the patients gave histories of renal calculi. Most of the authors noted the classic sign of increased hematuria following ureteral catheterization. A significant factor noted in this case was the presence of a typical lacuna in the roentgenographic silhouette of the ureter after injection of an opaque substance. The shadow had the typical form of a champagne goblet. Shadows of this kind are not observed in cases in which multiple papillomas are metastatic from a renal tumor. Most of the other primary ureteral tumors mentioned in

18. Parker, G.: Un papillome primitif de l'uretère, J. d'urol. **45**:38-44 (Jan.) 1938.

the literature were adenopapillomas or malignant epithelial tumors. Tumors of mesodermal origin (leiomyomas and fibromas) are also found.

Stone.—Alyea [19] stated that the principles employed in cystoscopic removal of ureteral calculi are dilatation, lubrication and anesthetization of the ureter and dislocation, grasping or crushing of the calculus. The most widely used procedures are manipulation with catheters, bougies, spiral corkscrew stone dislodgers and cagelike instruments for grasping the calculus. The indications and contraindications for cystoscopic removal of ureteral calculi must be carefully considered before a decision is made.

Calculi may remain in the lower third of the ureter for several years without causing serious damage to the upper part of the tract. The calculi always have grooves in them or permit the urine to escape around them in some other way.

A series of 327 cases in which ureteral calculi were present were analyzed; in 72 per cent the calculi were removed cystoscopically.

A technic of catching the calculus with multiple twisted catheters was described. The idea of continued traction on the calculus by means of a simple apparatus was suggested.

The use of spinal anesthesia for ureteral relaxation at the time of extraction may be helpful.

Torsion.—Berry [20] reported a case of bilateral pelviureteral torsion associated with stenosis of the ureterovesical junctions and hydroureters; the patient was a boy 7 weeks of age. The condition was discovered at necropsy, and a cast was made of the urinary tract in order to present the features of the lesions as they appeared in vivo. A case of bilateral pelviureteral torsion has not heretofore been described in the literature.

Fistula.—Findlay [21] reported a case in which a ureterovaginal fistula was successfully repaired by combined vaginal and transvesical operation.

Ureterovaginal fistulas may be due to (1) congenital ectopic ureter, (2) obstetric injury or (3) surgical injury. A congenital ureteral opening into the vagina or vestibule cannot be regarded as a true fistula, since it is not acquired.

Obstetric injuries are not now common causes of ureterovaginal fistulas. Morris (1900) stated that the obstetric methods practiced in his time gave rise to numerous ureterovaginal and vesicovaginal fis-

19. Alyea, E. P.: Cystoscopic Removal of Large Ureteral Calculi, J. Urol. **40**: 83-100 (July) 1938.

20. Berry, J. V.: Bilateral Torsion of the Ureter: Case Report and Brief Review of the Literature, J. Urol. **40**:378-383 (Sept.) 1938.

21. Findlay, H. V.: A Uretero-Vaginal Fistula Successfully Repaired by Combined Vaginal and Transvesical Operation, J. Urol. **40**:384-389 (Sept.) 1938.

tulas. In the recent literature there are few reports of ureterovaginal fistula occurring in the practice of a qualified obstetrician, but in the presence of prolonged labor the same injury may occur.

The greatest number of ureterovaginal fistulas are directly attributable to some form of surgical accident. Because of his particular activity in this field the gynecologist is doubtless responsible for most of these injuries, which occur in the performance of either vaginal or abdominal pelvic operations.

Findlay reported the case of a woman aged 59 whose uterus was markedly prolapsed. Sixteen years previously she had undergone myomectomy and perineorrhaphy.

Vaginal hysterectomy was performed. This was followed by persistently flowing moisture in the vagina. Cystoscopic study revealed granulation tissue near the left ureteral orifice.

Vaginal examination through a defect in the vaginal fascia which easily admitted three fingers revealed a rather marked enterocele. This enterocele herniated about 2 inches (5 cm.) down into the vagina. The fistulous opening could be seen in the left vault of the vagina, at the end of the transverse scar of the vaginal hysterectomy, lateral to the enterocele. The fistula admitted a no. 6 ureteral catheter, which was passed easily to the renal pelvis, and a pyelogram was taken. The bladder was again filled with 400 cc. of methylene blue solution, but none appeared in the vagina; as a matter of fact, the fistula continued discharging clear, colorless urine.

Operation was performed in an effort to close the ureterovaginal fistula. At first another unsuccessful attempt was made to pass a catheter through the bladder and up the left ureter. Then a catheter was passed through the vaginal opening of the fistula up the ureter to the kidney, and after this was withdrawn another catheter was passed through the opening and into the bladder. It was hoped that if a catheter could be passed along the ureter from the bladder to the kidney, cystotomy could be avoided, but even a small catheter could not be passed in both directions through the fistulous opening. In view of this failure the fistulous tract was dissected through the vagina, and the vaginal mucous membrane and fascia were undercut so that the edges could be firmly approximated with a single row of black silk sutures rather deeply placed. Cystostomy was then performed, and a silver probe was passed up the left ureteral orifice, well beyond the ureteral stricture, which was just distal to the fistula. The probe was then lifted in order to elevate the bladder, and the intramural portion of the ureter was cut through with a cautery down to the silver probe. This cut was carried through the stricture back to the normal ureter. The bladder, muscle and skin were closed in layers around a Freyer tube, and a cigaret drain was placed in the space of Retzius.

The patient had an uneventful convalescence as far as her general condition was concerned. The ureteral catheter remained in place for sixteen days. The suprapubic tube was not removed until the twentieth day. A week after its removal the wound was completely healed, and the patient was up and about, with perfect control of urine.

BLADDER

Anomaly.—Ignatescu, Slobozianu and Athanasiu-Vergu [22] reported 2 rare instances of agenesis of the bladder, with ureters opening into the uterus. The patients were twin sisters. The fetuses, stillborn in the seventh month, each presented an abdominal eventration. Such an anomaly is due to primary defective formation of the urinary apparatus. The fetuses belong in the class of celosomian monsters. The lower part of the body and the lower limbs were well developed. The presence of genitourinary organs and the existence of limbs place them also in the class of aspalasomas. The malformations, which were multiple, were almost identical in the two fetuses. Each had lumbar spina bifida with myelomeningocele; in both the large intestine and the gallbladder were lacking. In 1 fetus both ureters and in the other a solitary ureter from a solitary kidney debouched into a well developed uterus, which, however, lacked a cervix. Each had one hydronephrotic kidney. In 1 fetus the other kidney was normal. In the other fetus the small intestine occupied the site of an agenetic kidney. The ureters were long, sinuous and distended.

The absence of a bladder has been observed by the authors in symmelians and in infants with a persistent cloaca.

The aplasia of the anterior region which gave rise to eventration and at the same time to anomalies of the urinary apparatus must be of the same nature as that of the posterior region, where it caused spina bifida. The anomaly in monsters of celosomian type consists in defective development of the somatopleures, which allows the abdominal organs to herniate.

Tumor.—Adams reported a case of endometriosis of the bladder. He stated that this condition frequently is confused with other vesical lesions, particularly with malignant tumor. The occurrence of an intramural tumor of the bladder, presenting a bluish, cystic appearance on its surface, frequently resembling a varix, in a case in which there is a history of periodic attacks of pain, frequency, hematuria and dysuria occurring in the course of menstruation is typical of endometriosis of the bladder.

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22. Ignatescu, M.; Slobozianu, H., and Athanasiu-Vergu, E.: Absence de la vessie et abouchement des uretères dans l'utérus chez deux jumelles, J. d'urol. **45**: 51-55 (Jan.) 1938.

Adams [23] reported the case of a woman 36 years of age. Salpingo-oophrectomy was performed on the right. At the same time a number of adhesions between the uterus and the bladder were noted. Several weeks after the operation the patient had severe dysuria. At that time cystoscopic examination disclosed an intramural tumor. Pelvic examination revealed a tumor in the region of the fundus of the bladder. Suprapubic cystotomy was performed, and a tumor of the bladder was found. The tumor was about 3 cm. thick and was free of pericystic involvement. The tumor was resected and the bladder closed. At a later examination it appeared that the patient was cured.

The symptoms of vesical endometriosis depend on the extent and situation of involvement of the bladder and also on the presence or absence of involvement of other pelvic organs; that is, on whether the vesical involvement is primary or secondary. The symptoms consist of frequency of urination, dysuria and hematuria, which appear several days before menstruation, persist during the flow and generally continue for a day or two after its cessation. Hematuria is seldom macroscopic and is present only during the menstrual periods. The symptoms are insidious in onset and show a progressive increase in severity. Usually a tumor is palpable on pelvic examination. If the tumor is secondary there will be other symptoms. The most prominent is acquired, progressive dysmenorrhea affecting a patient who is more than 30 years of age and who has no history of infection. There are usually definite but not characteristic abnormalities in the menstrual flow. The pelvic findings in well marked cases are similar to those of chronic pelvic inflammation.

The symptomatic triad frequency, dysuria, and hematuria occurring cyclically with menstruation, together with the presence of a pelvic mass, is suggestive of primary endometriosis of the bladder.

The cystoscopic findings are diagnostic in most cases if the examiner will keep in mind the possibility of endometriosis. The tumor usually involves the fundus, is about 2 to 4 cm. in diameter, is well circumscribed and is slightly or moderately elevated from the vesical wall, depending on the amount of vesical distention. The mucous membrane of the bladder is intact over the surface of the tumor, and the tumor itself is rather soft. The tumors are single and seldom undergo ulceration.

Treatment is variable and depends on many factors. As bilateral oophorectomy or irradiation of the ovaries removes the hormonal stimulation necessary for continued growth of a heterotopic endometrioma, artificial menopause would seem indicated if the patient is at or near the menopause or if involvement of the bladder is too advanced for

23. Adams, P. S.: Endometriosis of the Bladder: Report of a Case, J. Urol. **40**:390-396 (Sept.) 1938.

successful complete removal of the growth. For the primary type of tumor, excision of the vesical lesion is the method of choice in treatment of young women who are desirous of having children. Even for the secondary types of endometriosis of the bladder excision may be done, with a good chance of nonrecurrence.

Kirwin [24] stressed the necessity for careful study of the size, situation, histologic structure and stage of advancement of vesical tumors as a basis for selection of proper treatment. Three distinct types of treatment are employed, either separately or in combination: operation, diathermy and irradiation.

Only 23.4 per cent of vesical tumors are so situated that they can be removed by segmental resection of the bladder. Despite the increase in the number of cases in which total cystectomy is performed for carinoma, Kirwin said that any operation involving ureteral implantation is unjustified if the patient is elderly or enfeebled and that at best the outcome of such a procedure is highly uncertain.

Although diathermy is employed routinely in treatment of benign growths, it never has been satisfactory when used alone in treatment of malignant growths. Radium and roentgen therapy, although valuable adjuncts to other methods, are also unsatisfactory when used alone. No one method can be adapted to all cases.

Kirwin outlined various combinations of all three methods which will fulfil the requirements of conservative practice in the great majority of instances. They are listed as: (1) resection using clamps; excision by scalpel, followed by high voltage roentgen therapy; (2) resection by cautery knife, with implantation of radon seeds before the wound is closed; (3) fulguration by loop and disk electrodes through a suprapubic incision, followed by implantation of radon seeds, and (4) a closed method (removal of the exuberant portion of the growth by the resectoscope, followed by intraurethral implanation of radon seeds and in some cases by external roentgen therapy).

Diverticulum.—Ward [25] reported 53 cases of vesical diverticulum. The average age of the patients was 57 years; the youngest patient was 15, the next older 18 and the next 32; 10 were in the forties, and the oldest was 80. All were males except 1, who suffered from urethral stricture and whose diverticulum was not yet large enough to require resection. In only 2 cases could the diverticulum be considered of congenital origin; in 1 of these the patient was a boy aged 15 years.

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24. Kirwin, T. J.: The Management of Bladder Tumors, Surg., Gynec. & Obst. **66**:999-1007 (June) 1938.

25. Ward, R. O.: Fifty-Three Cases of Vesical Diverticula, Brit. J. Surg. **25**:790-815 (April) 1938.

A vesical diverticulum does not give rise to any unique symptoms, and only rarely can its presence be detected on general physical examination. The patient is commonly unaware that anything is wrong with him unless the urine becomes infected or until increasing difficulty or frequency of micturition arouses his interest.

Frequency of micturition is the commonest symptom and is not due so much to the diverticulum itself as to associated cystitis or prostatic enlargement. Pain on micturition is the next most usual symptom and is also commonly due only to cystitis. In this series infection was present in all but 2 cases. Difficulty of micturition undoubtedly is the most characteristic symptom. Thirty-six patients suffered from it, and of this number 14 either had retention of urine or had suffered from it intermittently. Such difficulty is not necessarily due to the presence of a diverticulum, for in 30 of these cases prostatic obstruction also was present.

In this series of 53 cases diverticulectomy alone was performed in 15 instances; diverticulectomy combined with treatment of prostatic obstruction, either by prostatectomy or periurethral resection, in 21 instances, making a total of 36 cases in which diverticulectomy was performed. There was 1 death immediately after diverticulectomy. One patient died after the second stage of prostatectomy. Two patients died after cystostomy. One, who had multiple small diverticula that had not been subjected to treatment, died because one of these diverticula was ruptured when a Bigelow evacuator was being used after a vesical calculus had been crushed. Litholapaxy never is employed when diverticula are of large or moderate size, because of the obvious impossibility of recovering the fragments of the calculus. This case is included in order to show that in the presence of even small pouches litholapaxy carries a risk which is not well recognized. One patient died three months after diverticulectomy and prostatectomy; 1, three weeks after periurethral resection of the prostate gland; 1, twenty months after diverticulectomy; 1, four and one-half years after diverticulectomy and prostatectomy (of apoplexy), and 1, twelve years after the operation, of another disease. The other patients, as far as can be ascertained, are alive and well.

Paralysis.—Ferguson and Watkins [26] discussed paralysis of the bladder and associated neurologic sequelae of spinal anesthesia (cauda equina syndrome).

From time to time there have appeared in the literature reports of cases in which neurologic complications—varying from headache, menin-

26. Ferguson, F. R., and Watkins, K. H.: Paralysis of the Bladder and Associated Neurological Sequelae of Spinal Anaesthesia (Cauda Equina Syndrome), Brit. J. Surg. **25**:735-752 (April) 1938.

gism, cranial nerve paralysis and focal cerebral lesions to radiculomyelitis and lesions of the cauda equina and the peripheral nerves—have occurred immediately or remotely after administration of a spinal anesthetic agent.

The authors recorded 14 cases in which a cauda equina syndrome developed after administration of a spinal anesthetic agent. Thirteen of these cases were observed within twenty months. Only 16 examples of this lesion were found in examination of the literature published before this period.

In the cases recorded by Ferguson and Watkins, almost immediately after the spinal anesthesia the following manifestations occurred: retention of urine, succeeded by incontinence; incontinence of feces with loss of anal sphincteric tone; impairment of sensation in the "saddle" area and in some cases also down the back of one thigh, and absence or diminution of one ankle reflex (occasionally absence of both ankle reflexes and even of the knee reflexes). It was clear from examination of all these patients that the basic lesion was the same but that the variations were due to different degrees of the same syndrome.

The vesical symptoms nearly always appeared within twenty-four hours of the operation, whereas rectal symptoms sometimes were delayed —in 1 case for ten days—almost suggesting a progressive lesion. Complete urinary retention developed after operation in all except 1 case, that of a female whose only apparent vesical disturbance was incontinence on one occasion. The period of complete retention varied from about a week to a month and was followed by incontinence of urine. Incontinence usually was of short duration (a few weeks) but in 2 cases was still present after more than two years. In the early stages of spontaneous urination there was always marked frequency of voiding. In 1 case this subsided in about 6 weeks; in 2 it passed off in six months, and in 4 others it was still troublesome for periods varying from nine to twenty-seven months after operation. Residual urine persisted for from six to twelve months or more and in 1 case was still present after twenty-seven months.

A sensation of numbness—at first constant and after about a year intermittent—in the saddle area was a universal complaint. This numbness was still present in some cases three years after the operation.

It is evident that the lesion under discussion is the direct result of administration of the spinal anesthetic agent, since in all cases it appeared immediately after operation. The clinical manifestations of the lesion might be explained either by damage to the lumbosacral portion of the cord or to the conus medullaris on the one hand, or to the nerves of the cauda equina on the other. For several reasons, however, it seems more probable that the maximal damage is to the latter.

Of the 14 cases in this series, the difficulty in 13 definitely followed employment of a heavy solution of the drug known as "duracaine" (a pseudohypobaric solution of procaine hydrochloride). It is probable, but not certain, that this drug also was utilized in the remaining case. Thirteen of these cases were observed in the Royal Infirmary in Manchester, England, 12 within a period of twenty months. During this period, about 1,000 instances of spinal anesthesia induced with "heavy" durocaine were reported in the hospital records. In addition, the records for this period include 650 instances of spinal anesthesia in which the drug is not named and 60 cases in which a light solution of durocaine was employed. The total number of cases in which durocaine was the anesthetic agent must, therefore, be between 1,000 and 1,700, giving a rate of incidence for this lesion of between 1 in 90 and 1 in 155 (if the doubtful case is included).

During the period from July 1933 to December 1935, stovaine (benzoyldimethylaminomethylpropanol hydrochloride) was administered at the Manchester Royal Infirmary 1,000 times and nupercaine 300 times (in addition to cases in which the anesthetic used was not mentioned). No case of paralysis was observed in this group.

Rupture.—Gaston [27] stated that trauma, not infrequently associated with alcoholism, is the commonest etiologic agent encountered in cases of intraperitoneal rupture of the bladder.

The laceration of the vesical wall usually runs in an anteroposterior direction across the dome of the bladder. Because of the obstacles to exposure, adequate closure of the posterior extremity of the laceration often is difficult.

A discussion of the special test whereby the diagnosis of intraperitoneal rupture of the bladder can be definitely established was presented.

Treatment of intraperitoneal rupture of the bladder is purely surgical and should encompass three aims: (*a*) treatment of the laceration of the vesical wall, (*b*) treatment of the peritoneum and (*c*) establishment of adequate drainage of vesical urine. A discussion of these factors and their relative importance was presented.

The mortality is directly proportional to the time which elapses between rupture and institution of adequate surgical treatment.

Wyatt and Douglass [28] reviewed the literature and presented 31 cases of spontaneous rupture of the tuberculous urinary bladder. In

27. Gaston, E. A.: Intraperitoneal Rupture of the Urinary Bladder, New England J. Med. **218**:958-963 (June 9) 1938.

28. Wyatt, T. E., and Douglass, H. L.: Spontaneous Rupture of the Tuberculous Bladder, J. Urol. **40**:506-512 (Oct.) 1938.

all cases of intraperitoneal rupture death occurred in spite of surgical intervention. Attempts at repair of 4 vesicovaginal fistulas of tuberculous origin failed.

The authors reported a case of spontaneous tuberculous vesicovaginal fistula of three months' duration. After nephrectomy and subsequent irrigations of the bladder with a weak solution of phenol the fistula healed almost spontaneously.

They concluded that spontaneous rupture of the tuberculous bladder is rare. Intraperitoneal rupture is more common than extraperitoneal fistula. Nephrectomy in the presence of unilateral renal tuberculosis, nephrostomy and ureteral transplantation are the only means of treatment. In the authors' opinion the prognosis of tuberculosis of the urinary tract depends more on the severity of the cystitis than on the degree of nephritis. After operation the cystitis must be controlled before the patient can recover.

Hernia.—Gayet and Cavailher [29] reported an unusual case of right inguinal hernia of the ureter and bladder. The patient, a very obese man aged 68, for many years had had an enormous, irreducible hernia in the right groin, which in the course of years had reached the size of the head of an adult human being. For several years he had suffered with attacks of hematuria and dysuria and had observed that often he could accomplish a difficult urination by making pressure on the hernia. An attack of complete retention of urine brought him under the authors' observation.

Catheterization proved impossible, the catheter stopping at the neck of the bladder. In the belief that a large part of the bladder, if not the entire organ, was in the abdomen, cystostomy was performed very low, behind the symphysis pubis. This elicited only a little gravel and a few drops of urine. The patient died on the following day.

At necropsy an enormous thick-walled sac was observed descending to the base of the scrotum; this proved to be the bladder itself, a flabby ovoid pocket containing but little urine. At the level of the very wide internal inguinal ring it became reduced to a sort of isthmus which continued into the abdomen for 3 to 4 cm., where it became prolonged into the urethra. It was completely inverted, so that the cystostomy wound, supposedly made in the anterior surface, was seen to be on the prolapsed posterior surface. Behind the bladder was observed the greatly dilated ureter, which was at first mistaken for an intestinal loop; most of it (15 to 20 cm.) was in the sac, which contained no intestinal loops. The right kidney was low, at the level of the crest of the ilium; at its

29. Gayet, G., and Cavailher: Hernie inguinale droite de l'uretère et de la vessie, J. d'urol. **45**:193-198 (March) 1938.

superior pole there was a small bluish subcapsular cyst; the calices, the pelvis and the upper portion of the ureter were greatly distended. The left kidney was small and atrophic; the left ureter was normal.

Had it been possible to guess during life that the hernia consisted solely of the bladder and the greater portion of the ureter, it would have been simpler to make a puncture or a small incision that would have revealed the bladder within the scrotum and thus to establish a temporary opening to drain it. In the absence of this knowledge, however, the risk of finding the intestinal peritoneum within the hernia was too great. Even if a correct diagnosis could have been reached, reduction of such a hernia, reintegration of the ureter and closure of the hernial orifice constituted too long and laborious a procedure to be borne by a patient who was desperately ill and whose renal function was so defective.

Stone.—Wildbolz and Kohlschütter [30] stated that careful observation concerning spontaneous disintegration of vesical stones in man may perhaps lead to better treatment for stone in the urogenital tract. If the physician succeeds in most cases in determining the causes of spontaneous disintegration of stones, he may be able to fulfil the desire of patients and of physicians to remove even large stones without operative procedure.

Most stones which undergo spontaneous destruction are pure urate stones (75 per cent), associated with infected urine, and most of them are vesical stones; rarely are they renal stones.

Wildbolz and Kohlschütter gave an accurate review of their examination of pure urate stones which had undergone spontaneous disintegration. They concluded that the structure of the stone is chiefly responsible for the possibility of its disintegration and that the structure depends on the manner of its formation.

Reconstruction.—Friedrich [31] discussed the procedure of forming a new bladder from the intestine. In 4 cases of shrunken, contracted bladder he anastomosed a ring of small intestine and the bladder proper. He encountered no unusual operative difficulties. In 2 cases the results were excellent, and urination became normal. In the other 2 cases, although the capacity of the bladder increased to normal, there was no relief of symptoms referable to the urinary tract. He stated that this was probably due to the fact that the anastomosis was not sufficiently extensive and was too high at the vertex of the bladder, causing the intestine to act as a diverticulum.

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30. Wildbolz, H., and Kohlschütter, V.: Ueber Selbstzertrümmerung der Blasensteine, Schweiz. med. Wchnschr. **68**:872-875 (July) 1938.

31. Friedrich, H.: Ueber die Scheelesche Blasen-Dünndarmringplastik, Ztschr. f. Urol. **32**:420-424, 1938.

De Gironcoli [32] stated that many operations are required for the formation of a functioning intestinal bladder. Each operation carries a considerable risk, endangering the life of the patient without giving him relief from his symptoms or removing the diseased tissue. Even in cases in which an intestinal bladder is successfully formed there is no certainty that the patient will not have a descending infection of the urinary tract.

Incontinence.—Davies [33] stated that urinary stress incontinence, a disease peculiar to women, is caused by a disturbance of the urethral sphincters which makes them unable to retain urine when intra-abdominal pressure is increased. The condition may be caused by injury during labor to the bridge of musculofascial tissue between each two of the three openings of the pelvic outlet, the urethra, the vagina and the rectum; or it may be the result of general physical underdevelopment in women who are unable to cause the muscles of the abdominal wall to contract or who are unconscious of a voluntary sphincter of the rectum or vagina. They cannot exert sufficient pressure against the urethral canal to withstand increased abdominal pressure and prevent leaking.

Davies gave a new conception of the urethral sphincter of the female. The urethra is composed of two layers of involuntary muscle fibers and at its origin from the bladder is encircled by an additional hypertrophied layer of involuntary muscular fibers called the "internal sphincter." This mechanism is sufficient to retain urine in the bladder under ordinary circumstances. In addition, the action of the three muscular planes through which the urethra passes constitutes a voluntary sphincter which protects against leakage of urine when there is increased intra-abdominal pressure, such as occurs in laughing, coughing, aggressive intercourse or a fall.

The first muscular layer perforated by the urethra is the levator ani muscle, which, in the usual textbook descriptions, is represented as simply running lateral to it. As a matter of fact, fibers are supplied to the urethra and at times surround it for its entire length. When the levator ani muscle is contracted, the portion surrounding the urethra causes the urethra to undergo angulation anteriorly. The middle layer is the deep transverse perineal muscle which bridges the area bounded by the pubic arch, between the layers of the urogenital diaphragm.

32. de Gironcoli, F.: Eine Kritik zur künstlichen Harnblase, Ztschr. f. Urol. **32**:416-419 (June) 1938.

33. Davies, J. W.: Urinary Stress Incontinence: The Anatomical Defect Found and a Rational Method for Its Treatment, Surg., Gynec. & Obst. **67**:273-280 (Sept.) 1938.

This permits voluntary constriction of the urethra in its middle. The third layer is composed of the bulbocavernosus and the ischiocavernosus muscle, which lie lateral to the urethra but communicate anterior to it. They are not usually considered to be sphincters of the urethra, but their voluntary contraction results in posterior angulation of the distal portion of the urethra, just the opposite to the angulation produced by the levator ani at the proximal portion. This mechanism of voluntary sphincters acts as a protection against leakage by double angulation of the urethra and constriction of its middle.

Injuries to these sphincters during labor may result from tears or from ischemia. Treatment for urinary stress incontinence not caused by childbirth consists in development of the muscles through calisthenics and exercises of the levator as a whole. Attempts should be made to interrupt the urinary stream, and the vaginal sphincter should be intermittently contracted during intercourse. Venous stasis accompanying the condition is improved by assumption of the knee-chest position.

In cases in which there is anatomic damage, accurate reconstruction can be accomplished by first approximating the lacerated tissue of the base of the bladder. This repair when continued distally will result in reconstruction of the involuntary sphincter at the neck of the bladder and eventually of the levator ani muscle and the deep transverse perineal muscles. The superficial sphincter is reconstructed as the posterior perineal body is repaired. Of 50 patients with stress incontinence, 45 were cured by surgical treatment.

Purpura.—Meyer [34] described the clinical picture of purpura of the bladder and nonspecific ulcers of the bladder, surveying the literature and analyzing his own cases.

He had 23 patients with purpura and 52 patients with nonspecific ulcers of the bladder. In many instances it was found that the diseased condition of the bladder resulted from a focus of infection elsewhere. The vesical condition usually was improved by removal of these foci, even without local treatment, and even in cases in which most types of local treatment had been resisted healing could be brought about by eradication of the infection.

34. Meyer, E.: Zur Frage der hämatogenen Entstehung von Blasenpurpura und unspezifischem Blasengeschwür, Ztschr. f. Urol. **32**:369-392, 1938.

(To be concluded)